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CURRENT CANCER RESEARCH

on

OCCUPATIONAL AND ENVIRONMENTAL CARCINOGENESIS

OCTOBER 1981

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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CURRENT CANCER RESEARCH

I. CANCER INCIDENCE ASSOCIATED WITH SPECIFIC OCCUPATIONAL EXPOSURES

A. EXPOSURE TO ASBESTOS

1. STUDY OF A BRITISH SHIPYARD POPULATION WITH REGARD TO LUNG CANCER INCIDENCE IN MEN WITH PLEURAL PLAQUES

Edge, J. R., University of Newcastle upon Tyne, Postgraduate Department, *6 Kensington Terr., Newcastle upon Tyne NE1 7RU, England, United Kingdom*

Pleural plaques, both fibrous and calcified, have been widely described in the neighborhood of asbestos mines and in populations using asbestos industrially. They are commonly thought to be benign lesions merely indicating prior asbestos exposure. The present study concerns a shipyard population of 7,000 men who have been found to have a high prevalence of pleural plaques (one third of the male population as assessed in 100 consecutive unselected autopsies), and a substantial annual incidence of malignant mesothelioma of the pleura. The clinical impression is that the occurrence of bronchial carcinoma in men showing pleural plaques is substantially increased. A group of Barrow shipyard workers with pleural plaques and a matched group of Carlisle workers from different but non-asbestos-exposed occupations are being compared in a long-term mortality study. The results to date suggest an increased incidence of bronchial carcinoma in the men with pleural plaques of approximately five times that found in the control series. After elimination of the subjects showing bias, due to being obtained from clinic sources, a residual group of 231 subjects with plaques from Barrow, together with a matched group of 231 controls from Carlisle, has been flagged on the National Cancer Registry computer in Southport. Both groups will be followed for not less than five years unless a valid result emerges sooner. The increase in the incidence of bronchial carcinoma in the plaque group after this has been allowed for, is likely to be nearer twofold than the fivefold initially estimated.

2. HEALTH EFFECTS OF ASBESTOS EXPOSURE IN NAVAL SHIPYARD WORKERS

Kolonel, L. N., Hirohata, T. Y., Viola, F., University of Hawaii System, Manoa Campus, Cancer Center of Hawaii, Epidemiology Program, *1997 East West Rd., Honolulu, Hawaii*, 96822, United States of America

A retrospective cohort of 9,000 male shipyard workers employed at the Pearl Harbor Naval Shipyard in 1950, and subsequently through 1968, has been identified. Complete work histories have been obtained for each man, as well as records of environmental levels of asbestos. Follow-up of these men for their vital status as of 1974 is in progress. Mortality from all causes, respiratory diseases, and site-specific cancer will be compared with that expected based on the mortality experience of the Hawaii population of comparable age, sex and race. Smoking histories will be obtained from the living cohort in Hawaii, who will then be followed prospectively for morbidity and mortality over the next several years. The possible synergism between smoking and asbestos exposure in the risk of cancer will also be examined.

3. ROYAL NAVAL DOCKYARDS ASBESTOSIS STUDY - MORTALITY PROJECT

Rossiter, C. E., McMillan, G. H., Medical Research Council, Clinical Research Center, Division of Computing & Statistics, *Watford Rd., Harrow HA1 3UJ, England, United Kingdom*

The 6,292 men working in the Royal Naval Dockyards on Jan. 1, 1947 were followed up to the end of 1978. About 4 percent of all deaths could be related to exposure to asbestos and over half of these were mesothelioma deaths. The mortality of this group will continue to be studied because of the possible increase in the mesothelioma rate as the period since first employment in the Dockyard passes 40 years. The 40,000 men working in all four Royal Naval Dockyards in 1972/73 are also being followed to relate their mortality, including from lung cancer and mesothelioma, to history of asbestos exposure and smoking habits.

4. EPIDEMIOLOGY OF MESOTHELIOMA IN DOCKYARD WORKERS IN DEVONPORT, UNITED KINGDOM

Wagner, M. M., Wagner, J. C., McMillan, G. H., Darke, C., Medical Research Council, Pneumoconiosis Unit, Dept. of Pathology, *c/o Llandough Hospital, Penarth CF6 1XW, Wales, United Kingdom*

About 10 cases of pleural mesothelioma occur each year in workers previously exposed to asbestos in Devonport dockyard. This is a prospective study relating the disease to previous exposure and to histopathological and immunological changes. It is hoped to identify any high-risk groups within this population including those who have already developed some form of asbestos related disease.

5. MORTALITY IN CHRYSOTILE ASBESTOS TEXTILE WORKERS - IMPLICATIONS FOR HYGIENE STANDARDS

Peto, J., Doll, R., Kinlen, L. J., Imperial Cancer Research Fund, Cancer Epidemiology Unit, *9 Keble Rd., Oxford OX1 3QG, England, United Kingdom*

The eventual risk of developing mesothelioma, lung cancer or asbestosis at the current asbestos hygiene standard (2 fibers/ml in the UK) is not known. Dust levels were rarely measured more than 20 years ago, and more recent exposure has not yet caused a detectable excess of cancer. Dust measurements have been made routinely in this factory since 1951, however, and levels from 1933 to 1950 have been estimated. The principal objective is the study of dose and time relationships for mesothelioma and lung cancer, so that the eventual effects of low asbestos exposure can be predicted from the observed effects of relatively high exposures. 1,100 workers exposed for 10 or more years are being followed up through factory and national records. In addition, mesotheliomas in 25,000 previous and current employees are being traced by matching employment records with the UK National Mesothelioma Register to relate incidence to level of exposure and period and duration of employment. Employment records of mesothelioma cases and matched controls will be compared to assess the risks associated with particular processes in the factory.

6. COHORT STUDY OF ASBESTOS-RELATED ILLNESSES IN WORKERS PREVIOUSLY EXPOSED TO ASBESTOS IN A SALTPETER PLANT

Hilt, B., Langard, S., Telemark Sentralsjukehus, Dept. of Occupational Medicine, *Olavsgt. 26, 3900 Porsgrunn, Norway*

The study is designed as a retrospective and prospective mortality and morbidity cohort study on the effects of occupational exposure to asbestos in a saltpeter plant located in southern Norway. The cohort consists of all men directly and indirectly exposed to asbestos dust in two divisions of the plant, and who started work there between 1929 and 1970. This includes about 320 persons. Based on assumed different levels of exposure, the cohort is divided up into subgroups. Most of the still living 160 men have been subjected to a medical examination

which also includes a chest x-ray and simple spirometry. A detailed work history is taken from every man and respiratory symptoms are registered on a questionnaire (Medical Research Council, 1976). The cohort will be followed up by yearly examinations for a least five years. Occupational data on the dead members of the cohort are obtained from the plant's personnel department. Health data will be obtained from the plant's medical department, from the local hospital and from the Norwegian Cancer Registry. Data on smoking habits are collected from different sources and will be taken into consideration in the statistical calculations. The main aim of the study is to contribute to the design and justification of screening programs for former asbestos workers. It is also hoped to further knowledge on dose-response and dose-effect relationships.

7. MORTALITY, MEDICAL, AND INDUSTRIAL HYGIENE STUDY OF BRAKE LINING WORKERS (NCI)

Leffingwell, S., Robinson, C., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

The NIOSH recommended standard for asbestos exposure of 2.0 fibers longer than 5 microns per cubic centimeter of air was made with the recognition that: 1) health data were not available for exposures to low levels, and 2) definitive information on the biological response to different sized fibers was not available.

Industrial hygiene surveys have been conducted in eight automobile repair facilities by the Industrial Hygiene Section. Optical counting and electronmicroscopic analyses are being performed in order to characterize the nature of the exposures occurring in these types of operations.

A contract has been let to the Environmental Sciences Laboratory Mt. Sinai School of Medicine to evaluate health effects of exposure to asbestos-containing dusts in brakelining maintenance and repair. The contract consists of two evaluations: 1) a feasibility study, to locate a cohort of brakelining repair and maintenance workers with sufficient latency to conduct a retrospective mortality study of these workers; and (2) a cross-sectional medical survey, to define the current health status of a representative cross-section of workers occupationally exposed to brakelining dusts. In conjunction with the cross-sectional medical study, NIOSH has undertaken industrial hygiene assessments at a representative sample of work establishments. The cross-sectional medical survey final report is due September 30, 1979.

The cross-sectional medical study had considerably lower participation than anticipated. Additional work will be required to characterize non-respondents.

8. MORTALITY STUDY OF ASBESTOS FRICTION WORKERS

Newhouse, M. L., Berry, G., Skidmore, J., University of London, London School of Hygiene & Tropical Medicine, T.U.C. Centenary Inst. of Occupational Health, *Keppel St., London WC1E 7HT, England, United Kingdom*

This is an old, established plant chiefly devoted to the manufacture of brake linings. Apart from two periods of approximately two years each, more than 30 years ago, only chrysotile asbestos has been used. Identification data of current and past employees is available. With the assistence of the National Register the vital status of past employees will be established and the cause of death, as stated on the death certificate, ascertained. Mortality in this population will be compared with that of the population of England and Wales. Dust estimates are available only since 1969 but by means of simulation experiments dust exposure at various times will be estimated and a case-control study of deaths from lung cancer will be undertaken following the methods of Liddel and Macdonald. Tracing has now been completed and the vital status of approximately 98% of past employees established. Approximately 20% of the 13,000 past employees are deceased and the causes of death established.

9. A STUDY OF MALIGNANCY AND OTHER ASBESTOS-RELATED DISEASES IN RELATION TO CROCIDOLITE MINING AND ENVIRONMENTAL EXPOSURE AT WITTENOOM GORGE

Hobbs, M. S., Murphy, B., Armstrong, B. K., Musk, W. B., Elder, J., Shilkin, K., University of Western Australia, Unit of Clinical Epidemiology, *Nedlands, W. Australia 6009, Australia*

The aim of the study is to determine the incidence of mesothelioma, bronchogenic carcinoma and other malignant tumors in workers previously employed in mining and milling crocidolite at Wittenoom Gorge, Western Australia, between 1942 and 1966, in relation to duration of exposure and smoking habits. The risk of mesothelioma in the relatives of workers and other Wittenoom Gorge residents not directly involved in mining crocidolite will also be assessed. Work is continuing to determine the vital status and present whereabouts of approximately 6,500 men formerly employed at Wittenoom Gorge through electoral rolls, other population registers and cancer and death registers in different Australian States. Commencing in 1979 a questionnaire will be sent to all former Wittenoom Gorge workers so far located to obtain further details concerning occupation and smoking habits. Respondents will be followed for as long as necessary to determine the interaction between crocidolite exposure and smoking in relation to the development of bronchogenic carcinoma. This questionnaire will also seek information concerning relatives of former asbestos workers also living at Wittenoom Gorge. This will be supplemented, if possible, by information from local government and school records to establish a roll of persons not directly involved in processing crocidolite but possibly at risk of developing mesothelioma from environmental exposure. Procedures will be established to monitor this cohort for the future development of mesothelioma.

10. MORTALITY, MEDICAL AND INDUSTRIAL HYGIENE STUDY OF GOLD MINERS EXPOSED TO ASBESTIFORM MINERALS - NATIONAL CANCER INSTITUTE

Brown, D., Zumwalde, R., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Surveillance, Hazard Evaluations & Field Studies Division, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

The NIOSH recommended standard in 1972 for asbestos exposures of 2.0 fibers longer than 5 microns per cubic centimeter of air (fibers greater than 5 microns/cu.cm) was made with the recognition that health data for exposures to low fiber levels and definitive information on the biological response to different sized fibers were not available. NIOSH in 1976 recommended a standard of 0.1 fiber greater than 5 microns/cu.cm.

In 1976 NIOSH reported on a mortality study of a mining population exposed to amosite asbestos (cummingtonite-grunerite) concentrations below 2.0 fibers greater than 5 microns/cu.cm and with most fibers being shorter than 5 microns in length, that demonstrated significantly increased mortality due to both malignant and non-malignant respiratory disease.

The purpose of this project is to complete an expanded retrospective mortality study (contract), analyze the data, and prepare a final study report utilizing the results from the completed industrial hygiene and medical studies.

11. PREVALENCE OF ASBESTOSIS, PLEURAL CHANGES AND MALIGNANT NEOPLASMS IN BLACK EX-MINERS AND FEMALE COBBERS

Harrison, W. O., Webster, I., Talent, J., South African Dept. of Health, Welfare & Pensions, National Centre for Occupational Health, Dept. of Occupational Medicine, *P.O. Box 4788, Johannesburg 2000, South Africa*

In 1973 the National Research Institution for Occupational Diseases was approached to determine the state of health of ex-employees of the asbestos mining industries, especially those using Cape crocidolite. Based at the St. Michael's Hospital at Bathlaros, near Kuruman, in the North West Cape Province, a small clinic was established, staffed by a doctor, nurse and a driver who knew the country and were well known in it. With the assistance of the Bureau of Census and Statistics mining company records were investigated. By August 1977 some 1500 ex-employees had been traced. At present attention is concen-

trated on investigating a cohort of ex- and current employees exposed during 1957-1962.

12. ETIOLOGY AND PROGNOSIS OF PLEURAL CALCIFICATION

Partanen, T. J., Ahlman, K. R., Wiikeri, M., Hannunkari, I., Taskinen, E., Inst. of Occupational Health, Dept. of Epidemiology & Biometry, *Haartmaninkatu 1, SF00290 Helsinki 29, Finland*

This project concerns the asbestos-related aetiology of pleural calcification and, from the view point of cancer, the prognosis of these calcifications. The study of prognosis has been directed mainly towards mortality from neoplasms in a cohort of 608 persons with pleural calcification and 608 persons without such calcification at the start of follow-up. The cohorts were formed in 1972 in connection with compulsory chest radiography of the populations of three communities: one with an anthophyllite mine and mill, the other with an asbestos cement-plant and a third 'average' urban community. Persons working in these two plants have been identified. The cohorts were matched by age and sex and were between 20 and 74 years of age at that time. By the end of 1976, 18 deaths were observed from neoplasms in the calcification group, 14 in the reference cohort. For malignate neoplasms of the respiratory tract, the figures were 10 and 8, respectively, and, for the neoplasms of the lymphatic and haematopoietic system, 3 and 0. Follow-up will be extended at least until 1983.

13. LATENT PERIODS OF LUNG CANCERS IN CHRYSOTILE MINERS AND MILLERS

Liddell, F. D., McDonald, J. C., McGill University, Dept. of Epidemiology & Health, *3775 University St., Montreal, Quebec*, H3A 2B4, Canada

The aim of this study is to investigate the variation in period from first occupational exposure to death in 244 deaths from lung cancer up to the end of 1975 among males in the 'Quebec Asbestos Mortality Cohort' consisting of 10,939 men born 1918 through 1920 who worked for at least a month in the asbestos mines and mills of Quebec. Account will be taken of the full histories of exposure, incorporationg the proportion of each year the man was employed and the average concentration of asbestos, yearly, measured in fibers per cc, and complete smoking histories obtained by questionnaires already completed but requiring recording. Attention will also be paid to such matters as eras of birth and of death, and attempts will be made to cast light on the mechanisms of carcinogenesis.

14. MESOTHELIOMA AND OTHER MALIGNANT DISEASE IN CHRYSOTILE ASBESTOS FACTORY WORKERS

McDonald, J. C., McDonald, A. D., University of London, London School of Hygiene & Tropical Medicine, T.U.C. Centenary Inst. of Occupational Health, *Keppel St., London WC1E 7HT, England, United Kingdom*

Cohort mortality studies are being undertaken in three large, long-established asbestos plants in the USA. In two chrysotile only has been processed and in the third crocidolite and amosite also were used since 1925. The three cohorts, not yet finalized, each comprise some 5,000 persons. Those first employed from 1937 through 1959 are of primary interest but persons employed before 1937 will also be studied. In all three plants some environmental measurements are available from 1930 onwards. In one plant a detailed study has just been completed including recent fibre levels and estimates of the equivalent in fibres of past dust levels. The possibility of similarly investigating environmental measurements in the other two plants is being investigated.

15. INTERACTION BETWEEN SMOKING AND ASBESTOS EXPOSURE IN LUNG CANCER AMONG CHRYSOTILE MINERS AND MILLERS

Liddell, F. D., McDonald, J. C., Thomas, D. C., McGill University, Dept. of Epidemiology & Health, *3775 University St., Montreal, Quebec*, H3A 2B4, Canada

In the 'Quebec Asbestos Mortality Cohort', consisting of 10,939 males and 440 females born 1891 through 1920 who worked for at least a month in the chrysotile mines and mills of Quebec, there had been 4,463 male deaths to the end of 1975. Of these, 244 were due to lung cancer, and, for a study under the direction of Professor J.C. McDonald, four controls had been selected from the cohort for each lung cancer death; the controls were born in the same year as the case, but had survived to a greater age. Work histories have been verified and annual exposures to chrysotile calculated in terms of fiber concentrations times proportion of year worked. Smoking history questionnaires had been completed for the great majority and are being recorded. New methods for comparing the fits of several models of observable interactions of the combination of asbestos and smoking in causing disease will be applied, leading to the possibilities of (a) inferences concerning biological models of carcinogenesis, and (b) the estimation of the probabilities that any individual's cancer was due to smoking or to asbestos exposure or to other factors.

16. INFLUENCE OF SMOKING ON CAUSES OF DEATH AMONG ASBESTOS INSULATION WORKERS

Selikoff, I. J., Hammond, E. C., Seidman, H., City University of New York, Mount Sinai School of Medicine, School of Medicine, Dept. of Community Medicine, *1 Gustave L. Levy Pl., New York, New York*, 10029, United States of America

On 1 January 1967 the entire membership, 17,800 men, of the Asbestos Workers' Union in the U.S.A. and Canada was registered. Smoking habits were recorded at the time of registration. The entire group has been followed prospectively from 1967 and death rates are being calculated taking smoking into account. For smoking-specific rates, the current data derived from the American Cancer Society's Cancer Prevention Study are being utilized, since this gives smoking-specific death rates 1960-1972. By the end of 1975, more than 2,000 deaths had occurred. Analysis is being undertaken according to cigarette, pipe and cigar smoking, age at beginning to smoke, amount smoked, duration of employment and duration from onset of employment, as well as other parameters. Specific causes of death which are of interest include various types of cancer and asbestosis.

17. CANCER MORTALITY AMONG PERSONS EXPOSED TO LOW LEVELS OF CHRYSOTILE ASBESTOS IN THE MANUFACTURE OF ASBESTOS-CEMENT ARTICLES

McCullach, S. F., Mahathevan, R., James Hardie Industries Ltd., Occupational Health Services, *Grand Ave., Camellia, N.S.W. 2142, Australia*

At Ipoh in Malaysia a workforce exposed only to chrysotile asbestos and engaged in the manufacture of asbestos-cement products is being studied. Engineering methods changed negligibly from 1966 when the plant came into operation to the time when the airborne asbestos concentrations in the breathing zones of the workers were first measured in 1978. On this basis it is believed that in no case has any worker's exposure exceeded two fibers/ml. On a time-weighted average basis. The cumulative exposures of all present (approximately 400) and former (approximately 1,000) employees have been determined. Death Registers will be searched to discover the deaths of those who have died after leaving the workforce. Where available, hospital records will be searched and consideration given to amending the certified cause of death. Each case will be matched with a control for sex, age within five years and place of residence. Consideration of the certified cause of death in the light of hospital records will be conducted in ignorance of whether one is dealing with case or a control.

18. CARCINOGENIC RISK IN ASBESTOS-CEMENT INDUSTRY

Kogan, F., Guselnikova, N. A., Sverdlovsk Research Inst. of Hygiene of Labor & Occup. Dis., Dept. of Industrial Hygiene in Mining & Metallurgy, *Repin 2, Sverdlovsk 620014, Russia, Union of Soviet Soc. Republics*

This retrospective and, perhaps in the future, prospective study is to determine the comparative carcinogenic risk by type of dust inhaled by workers in different parts of asbestos-cement plants. There are three types of exposure - asbestos, which in this country is chrysotile, cement alone, and asbestos-cement. In the past, a minor fibrogenic potential for cement and asbestos-cement was established and compared to that of asbestos.

19. INDUSTRIAL HYGIENE AND MORTALITY STUDY OF CRUSHED STONE WORKERS

Costello, J., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Respiratory Disease Studies, *944 Chestnut Ridge Rd., Morgantown, West Virginia*, 26505, United States of America

As a result of finding asbestos fibers in crushed rock being quarried in Maryland, negotiations were started and are continuing with the National Crushed Stone Association for NIOSH to do a national mortality study of workers in this industry. Emphasis will be placed on causes of death related to cancer and pulmonary diseases, comparison being made with the US national average for white males, and with white females for each of the states in which a quarry is visited. If large numbers of black workers are found the control populations are adjusted accordingly. As an integral part of this study, the Environmental Investigations Branch will examine and characterize the four basic types of rock being quarried. Preliminary surveys have been carried out in several quarries and data have been collected from five quarries. Arrangements have been made to collect data in three additional quarries.

20. MORTALITY CHANGES AMONG ASBESTOS MILL WORKERS AND MINERS

Kogan, F., Guselnikova, N. A., Sverdlovsk Research Inst. of Hygiene of Labor & Occup. Dis., Dept. of Industrial Hygiene in Mining & Metallurgy, *Repin 2, Sverdlovsk 620014, Russia, Union of Soviet Soc. Republics*

During the 1960's and 1970's the dust in mills in the asbestos industry significantly decreased. The objective of this study is to ascertain the influence of the improved work hygiene conditions on the level of cancer mortality.

21. CANCER RISK IN MAINTENANCE WORKERS IN CHRYSOTILE-ASBESTOS ENRICHMENT MILLS

Kogan, F. M., Deminov, A. G., Guselnikova, N. A., Sverdlovsk Research Inst. of Hygiene of Labor & Occup. Dis., Dept. of Industrial Hygiene, *Repin 2, Sverdlovsk 620014, Russia, Union of Soviet Soc. Republics*

This retrospective study aims to determine the cooperative carcinogenic risk in men who worked as maintenance workers in asbestos mills and other persons who worked during 25 years in the same mills. The major objective is to ascertain the role of intermittent exposure to dust which characterizes maintenance work.

22. EPIDEMIOLOGICAL STUDY OF LARYNX CANCER

Miller, A. B., Burch, J. D., Howe, G. R., National Cancer Inst. of Canada, Epidemiology Unit, *12 Queens Pk. Cres. W., c/o University of Toronto, Toronto, Ontario*, M5S 1A8, Canada

OBJECTIVE: The study is designed to investigate the relative contribution of the known and suspected aetiological factors in laryngeal carcinoma. A prime focus of the study is on evaluating possible occupational causes, specifically asbestos exposure but also possibly other occupational factors such as exposure to nickel and nickel manufacturing processes. The study also investigates the relative contribution of smoking and alcohol consumption together with other factors to the development of laryngeal cancer.

APPROACH: The study is a case/control study with data on past events and exposures obtained from cases and controls by means of a detailed questionnaire. The study population consists of all newly diagnosed (as of March 1, 1977) cases with carcinoma of the larynx together with controls matched to cases by age, sex, and area of residence. All cases resident in southern Ontario together with those living in the Sudbury and North Bay areas are eligible for interview. Case acquisition will continue from March 1, 1977 through February 28, 1979.

PROGRESS: The study is currently in the second year of case identification and interview and after fourteen months of fieldwork a total of 130 case/control pairs have been interviewed. All questionnaires have been coded and have been entered on the NCIC Unit's computer for analysis.

23. INFLUENCE OF OCCUPATIONAL AND ENVIRONMENTAL ASBESTOS EXPOSURE ON MESOTHELIOMA INCIDENCE IN CONNECTICUT

Lewinsohn, H. C., Meigs, J. W., Teta, M. J., Raybestos-Manhatten Inc., *100 Oakview Dr., Trumbull, Connecticut*, 06611, United States of America

It has been reported, using Connecticut Tumor Registry (CTR) data, that the incidence of mesothelioma in Connecticut has exhibited a sizeable increase since 1935. A positive correlation with the State's total asbestos consumption and the results of an air monitoring program for asbestos concentrations in Connecticut have served to justify a more stringent ambient air standard for the State. The present study has been designed to re-examine the CTR identified cases with respect to: (1) quality of diagnosis, and (2) direct and indirect domestic and occupational asbestos exposure. Medical, demographic, and occupational data have been collected for 229 cases of malignant mesothelioma, 38 cases of non-mesothelioma pleural tumors, their respective spouses, and approximately 700 decedents from the Division of Health Statistics of the Connecticut Department of Health. Sources of information include the records of the CTR, death certificates, city directories, as well as computer linkage programs with the files of the Connecticut Motor Vehicle Department and with the files of Connecticut decedents. An asbestos product listing with its associated employer and industrial codes has been developed to indicate possible occupational asbestos exposure. A slide review is underway in order to examine the quality of diagnosis.

24. MALIGNANT MESOTHELIOMA OF THE PLEURA IN MONFALCONE

Bianchi, C., Brollo, A., Ospedale Generale Provinciale - Monfalcone, Serv. di Anatomia e Istologia Patologica, *Via Rossini 1, Monfalcone, Gorizia, Italy*

Ship construction and refitting has been associated with high incidence of pleural mesothelioma. Monfalcone, a town of 30,000 inhabitants near Trieste, is the site of important shipyards. In the past, particularly in the period 1920-40, naval production in Monfalcone was one of the largest in the world. At present the incidence of pleural mesothelioma in Monfalcone is unknown. The aim of this study is to collect and analyze all cases of malignant pleural mesothelioma diagnosed in Monfalcone district. Occupational history and data on smoking habits will be obtained from the patient or relatives by personal interview. Special attention will be paid to asbestos exposure from occupation or other sources.

25. EPIDEMIOLOGY OF MESOTHELIOMA IN ISRAEL (1973-80)

Lemesch, C., Steinitz, R., Wassermann, M., Katz, L., Ministry of Labour, Div. of Labour Inspection, *P.O. Box 915, Jerusalem, Israel*

In this study the occurrence of mesothelioma in Israel is being monitored. During the period 1960-72, only one mesothelioma was noted to have a definite occupational history of exposure to asbestos (Environ. Res. 12: 255-261, 1976) but, considering that the asbestos industry in Israel was established only in the early 1950s and that mesothelioma of occupational origin has been shown to have a relatively long latent period of about 20 years or more, it is possible that more cases of clear occupational origin will appear in the near future.

26. LONG-TERM FOLLOW-UP OF ALL WORKERS EXPOSED TO ASBESTOS IN NORTHERN IRELAND

Langlands, J. H., Simpson, M., Coyne, F. C., Belfast City Hospital, Respiratory Investigation Centre, *93 Lisburn Rd., Belfast BT9 7AB, Northern Ireland, United Kingdom*

The objectives are to see how the changing conditions of work with asbestos are affecting the incidence of asbestosis, carcinoma of the lung and mesothelioma and whether preventive measures being taken are effective. This is a continuation of work already published and entails examining all men still at work and all men who have worked with asbestos in the past at 2-3 year intervals. If they develop illnesses or die, every effort is made to document precisely the nature of the illnesses or cause of death.

27. CANCER AMONG HOUSEHOLD CONTACTS OF ASBESTOS WORKERS

Anderson, H. A., Selikoff, I. J., Hammond, E. C., Churg, J., City University of New York, Mount Sinai School of Medicine, School of Medicine, Dept. of Community Medicine, *1 Gustave L. Levy Pl., New York, New York,* 10029, United States of America

The increased cancer risk (lung, pleural, mesothelioma and colon) associated with direct occupational exposure to asbestos has been well documented. Growing evidence of an increasing prevalence of asbestos associated disease among 'bystanders' (non-asbestos trade employees working in close proximity to asbestos workers) is being described. Concern has been extended to members of asbestos worker households (over 70 mesotheliomas reported in the literature). The current study will be the first to systematically examine the mortality experience of a well defined cohort of household members of amosite asbestos workers. During Year I, cohort workers were identified utilizing pre-existing records. Year II has been spent tracing the cohort and establishing vital status. The cohort now contains 2,205 members; all but 511 (23%) have had their vital status determined. Of 1,694 whose status has been updated, 1,164 are known alive and 620 deceased. Death certificates are being gathered and 553 have been obtained. Available information has been transcribed onto computer readable cards. Where death certificates indicate that death occurred in a hospital, and especially for those on whom a post-mortem was performed, written permission has been sought to acquire this information. Identification, tracing and updating of the cohort is proceeding as scheduled and is expected to reach 95% of the cohort.

The information from this study, when combined with the experience of index workers who have been occupationally exposed to the same fiber, from the same source, in the same years and geographical location, will make it possible to establish risk levels for these various asbestos exposures. It should also indicate whether the risk of household asbestos exposure warrants consideration by government, labor and industry and any proposed for surveillance of asbestos exposed individuals.

28. AN EPIDEMIOLOGICAL STUDY OF LEUKEMIA INDUCED BY EXPOSURE TO DIFFERENT CHEMICALS

Aksoy, M. B., Erdem, S., Koray, D. A., Guencag, D., Istanbul Universitesi, Faculty of Medicine, Internal Clinic, *Bayezit, Istanbul, Turkey*

Despite the fact that there is a significant reduction in the incidence of haematopoietic insults, such as aplastic anaemia and leukaemia, after the strict prohibition of the use of benzene as a solvent in Turkey, other chemicals (those used in the textile industry and asbestos) may still be involved in the occurence of leukaemia among the working population. The scope of the present project is to perform an epidemiological study as well as clinical and laboratory investigations directed towards the detection of the incidence and the types of leukaemia produced in those chronically exposed to these chemicals. It is also believed that the detection of the patients involved, while they are still at the pre-leukaemic stage, may be of importance. The cytochemical and immunological alterations likely to be observed in such subjects constitute another interesting aspect of the task. Chromatographical analysis of the chemicals in question will be undertaken.

29. MORBIDITY AND MORTALITY FROM PLEURAL MESOTHELIOMA - A RETROSPECTIVE CASE STUDY OF ASBESTOS EXPOSURE

Haider, M., Neuberger, M., Raber, A., Universitat Wien, Inst. of Hygiene, Social Medicine & Epidemiology, *Kinderspitalgasse 15, 1095 Vienna, Austria*

OBJECTIVE: To find risk factors for pleural mesothelioma.

APPROACH: Two hundred and thirty-six cases reported to the central Austrian cancer register (morbidity data) during 1969-1974 as 'primary malignant pleural tumors' were analysed. Some additional mesothelioma cases were detected through hospital statistics (data from pneumologic centers, autopsy statistics, etc.) and also the statistics of occupational asbestos related diseases (since 1938) were inspected. Information on each individual case was obtained from hospitals, family doctors, family members, fellow workers, employers and accident insurance companies. Main concern was the detection of occupational contact with asbestos.

PROGRESS: Preliminary resports have been published (Deutsch-Osterr.-Schweiz.-Unfalltagung Berlin 1975, in: Hefte zur Unfallheilkunde, 126, 547-549, 1976).

The first comprehensive report is due in September 1979

These studies are ongoing and will be continued.

BIBLIOGRAPHIC REFERENCES: Inst. Environmental Hygiene, University Vienna, Austria. New Approaches to Risk Estimation of Air Pollutants, Ed. Facultas, Vienna, 1979-December, ISBN 3-85076-079-0, pp. 117.

30. LUNG CANCER MORBIDITY IN WORKERS EXPOSED TO INDUSTRIAL CHEMICALS

Maties, R., Modorcea, V., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Medicine, *Strada Biserica Amzei 29, Bucharest, Romania*

The aim of the study is to evaluate the relation between lung cancer and occupational exposure to chromium salts and asbestos. Parameters of exposure which may have an influence on morbidity levels are identified and the relation of possible risk factors other than occupation (smoking habits, residence, previous morbidity) to lung cancer morbidity examined. The project consists of a retrospective study on lung cancer morbidity and mortality among workers exposed to asbestos and bichromates in two plants which have been in operation for more than 30 years, and a prospective follow-up of workers actually exposed. The results of periodical screening (standard chest radiographs, sputum cytology, clinical examination) are recorded and offer a comprehensive description of the changes in the health status.

31. MORBIDITY AND MORTALITY PATTERNS AMONG OCCUPATIONALLY EXPOSED ASBESTOS WORKERS (ABBREV)

Lemen, R. A., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

Considerable controversy has arisen concerning the validity of true exposure to chrysotile asbestos and its relative importance in the etiology of mesothelioma. Animal experimental evidence is contradictory. One study indicates that Canadian and Rhodesian chrysotile asbestos is the least carcinogenic fiber for mesothelioma, while another study has shown no fiber difference. This investigation will evaluate the risk of mesothelioma from exposure to chrysotile asbestos. It will also evaluate the usefulness of cross-sectional medical data perimeters as indicators of future asbestos-associated disease, e.g., lung cancer, mesotheliomas, gastrointestinal cancer, etc. A prospective analysis of tobacco usage (smoking of cigarettes, pipes, cigars and tobacco chewing) obtained through cross-sectional medical studies will be evaluated in those workers known to have died as a result of lung cancer, mesothelioma and gastrointestinal cancer.

32. DOCUMENTATION OF OCCUPATIONAL DISEASES

Versen, P., Berufsgenossenschaft der Chemischen Industrie, *Gaisbergstrasse 11, 6900 Heidelberg, Federal Republic of Germany*

Registration and analysis of occupational cancer with special attention to asbestos and vinyl chloride. Since 1975 such data have been registered according to an electronic data processing protocol in order to provide an analysis of the development of these diseases.

B. EXPOSURE TO ORGANIC CHEMICALS

1. MONOMERIC AND POLYMERIC VINYL CHLORIDE

33. CANCER MORTALITY AMONG VINYL CHLORIDE WORKERS IN SHAWINIGAN, QUEBEC

Theriault, G. P., Allard, P., Cordier, S., Iturra, H., Universite Laval, School of Medicine, Dept. de Medecine Sociale et Preventive, *Ste. Foy, Quebec,* G1K 7P4, Canada

This retrospective cohort study aims to determine cancer mortality patterns among workers employed in a vinyl chloride polymerization plant, Shawinigan, Quebec, and establish their

relationship with age, duration and level of exposure and alcohol and tobacco consumption. All workers employed during at least 5 years from the operative start of the plant until 31 December 1976 will be included. Their life status at the end of the study period, and the cause of death for the deceased, as well as duration and level of exposure to vinyl chloride and alcohol and tobacco consumption, will be determined. These data will be obtained through a questionnaire applied to the worker, or his family if he is dead. The industry, Population Registry and pathologists will also contribute relevant data. Values so obtained will be compared with those for a cohort of workers in the same firm who were not exposed to vinyl chloride. Cancer death rates will almost be compared to Quebec rates for the same period.

34. PROSPECTIVE STUDY IN RELATION TO OCCUPATIONAL EXPOSURE TO VINYL CHLORIDE

Tuinman, C. P., Ottevanger, C. F., Shell Nederland Raffinaderij B.V., *Vondelingenweg 601, Rotterdam, Netherlands*

Vinyl chloride (VC), under normal temperatures and pressures of gas, can easily be polymerized to polyvinyl chloride (PVC), a white solid material. Apart from fire and explosion risk and a quickly appreciated narcotic effect, acro-osteolysis and soft tissue changes have also been described. Following an epidemiological study by Maltoni in 1974, reporting a cluster of cases of angiosarcoma of the liver in men who had previously worked as cleaners of reactors, a prospective study on VC-workers in this polymerization plant has been set up, comprising the tracing of medical data on previous VC-workers and a biannual physical and biochemical investigation of the present VC-population. Findings are related to the degree of VC-exposure as measured either by personal monitoring or fixed point air sampling.

35. CANCER EXPERIENCE OF VINYL CHLORIDE POLYMERIZATION WORKERS

Selikoff, I. J., Nicholson, W. J., Hammond, E. C., Seidman, H., Popper, H., City University of New York, Mount Sinai School of Medicine, Dept. of Community Medicine, *1 Gustave L. Levy Pl., New York, New York,* 10029, United States of America

During 1974, over 1,200 vinyl chloride polymerization workers were examined in a clinical survey, and a great deal of clinical, biochemical, x-ray and pulmonary function data recorded. In addition, details concerning vinyl chloride and other chemical exposures were noted, with complete occupational histories (including other than vinyl chloride employment). This cohort of vinyl chloride-exposed workers (approximately 1/5 of the vinyl chloride polymerization workers employed in the U.S.) is being observed prospectively. Their mortality experience will be analyzed and compared with expected deaths by cause.

36. CANCER INCIDENCE AMONG VINYL CHLORIDE AND POLYVINYL-CHLORIDE WORKERS

Storetvedt Heldaas, S., Langard, S., Norsk Hydro, Dept. of Health, *3900 Porsgrunn, Norway*

The aim is to evaluate whether workers exposed to vinyl chloride have an increased risk of developing cancers other than angiosarcoma of the liver. In a historical study, the mortality and cancer incidence among workers producing polyvinyl chloride since 1950 is followed from 1950 through 1978. A complete working history for all members, some 1,400, of the population is recorded and they are characterized according to levels of exposure. The mortality rates for similar age-groups in the Norwegian population are used to compare mortality. As a reference for cancer incidence, rates for both the total Norwegian population, a local population and an internal population consisting of workers employed for a short period are being used.

37. MORTALITY STUDY OF VINYL CHLORIDE WORKERS

Nakamura, K., Sakabe, H., National Inst. of Industrial Health, Dept. of Industrial Epidemiology, *2051 Kizuki Sumiyosityo, Kawasaki, Kanagawa, Japan*

A mortality study is being undertaken for about 10,000 workers who are or were engaged in vinyl chloride (monomer and polymer) manufacturing processes in Japan to ascertain the relationship between exposure to vinyl chloride monomer and liver angiosarcoma. Ascertainment of deaths is obtained by a family registry system and causes of death are determined from death certificates and clinical records. So far, one case of liver angiosarcoma has been confirmed.

38. EPIDEMIOLOGY OF HEPATIC ANGIOSARCOMA

Falk, H., Thomas, L. B., Popper, H. A., Telles, N. N., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, Bureau of Epidemiology, Cancer & Birth Defects Division, *1600 Clifton Rd. N.E., Atlanta, Georgia,* 30333, United States of America

This project started about four years ago with the discovery of the association between hepatic angiosarcomas and long-term exposure of industrial workers to vinyl chloride. Subsequently, a survey of pathologists in the USA was conducted and to date about 250 cases of human hepatic angiosarcoma have been identified and the slides reviewed. As noted, some of these cases were caused by vinyl chloride. Other cases were caused by or associated with exposure to Thorotrast or to arsenical compounds. The majority of the cases have no known environmental or industrial aetiology. The epidemiological study which is continuing involves obtaining detailed work and exposure histories from all these patients or from their living relatives. The pathological aspects of the study are conducted by Drs. Thomas, Popper and Teller. The epidemiological aspects are under Dr. Falk and other epidemiologists at the Center for Disease Control in Atlanta, Georgia.

39. IS ANGIOSARCOMA OF THE LIVER ASSOCIATED WITH VINYL CHLORIDE MONOMER EXPOSURE IN SOUTH AFRICA?

Webster, I., Bougas, T., Dalton, J. P., Irwig, L. M., South African Medical Research Council, National Research Inst. for Occupational Diseases, *Joubert St. Ext., P.O. Box 4788, Johannesburg 2000, Transvaal, South Africa*

In South Africa the main producer of polyvinyl chloride plastic has two factories. It has been manufactured at Umbogintwini since 1950, but at the Midlands factory for only eight years. The present labor force is being monitored by liver tests and clinical and radiological examinations. Ex-employees are being traced, especially those from Umbogintwini, in whom, if they were exposed to vinyl chloride monomer, the possible latent period of 20-30 years has now been reached.

40. MORBIDITY SURVEY IN RELATION TO OCCUPATIONAL EXPOSURE TO VINYL CHLORIDE

Tarpa, A., Camarzan, D., Ivanescu, M., Eftimescu, M., Spiru, M., Ministry of Chemical Industry, Labour Protection & Hygiene Centre, Dept. of Prevention of Occupational Diseases, *59 Pop de Basesti, 73244 Bucharest 3, Romania*

Since 1975, over 700 workers exposed to vinyl chloride at three industrial plants in Romania have been examined every year. The survey entails health questionnaires, medical examinations, biochemical, immunological and other health indices, such as respiratory and X-ray investigations and genetic studies. Serum are estimated AFP and CEA. The aim of this study is to define the general effects (including carcinogenic properties) of vinyl chloride exposure.

41. ANGIOSARCOMA OF THE LIVER

Duncan, K. P., Health & Safety Center, *97 Horseferry Rd., London SW1P 2DY, England, United Kingdom*

All deaths from angiosarcoma of the liver in the UK are verified by supplying pathological material to a panel of pathologists. Those confirmed by the panel are investigated for occupational exposure to vinyl chloride.

42. VINYL CHLORIDE - RISK AND ONCOGENESIS

Ribacchi, R., Cristallini, Universita degli Studi di Perugia, Istituto di Anatomia e Istologia Patologica, *Colle Obito, 05100 Terni, Italy*

OBJECTIVE: As Terni is the industrial centre of Umbria, research will be carried out on the cancer risk to which vinyl chloride workers are exposed. The incidence and type of cancer produced will be investigated.

As this research is in the early planning stages, no further information can be given at this moment.

43. DOCUMENTATION OF OCCUPATIONAL DISEASES

Versen, P., Berufsgenossenschaft der Chemischen Industrie, *Gaisbergstrasse 11, 6900 Heidelberg, Federal Republic of Germany*

The summary for this project is under entry no. 32.

2. OTHER CHLORINATED ORGANIC COMPOUNDS

44. CASE-CONTROL STUDY OF MALIGNANT MELANOMA

Bahn, A. K., University of Pennsylvania, School of Medicine, Dept. of Research Medicine, *36th & Hamilton Walk, Philadelphia, Pennsylvania*, 19174, United States of America

This is a two-year case-control study of 225 cases and matched controls resident in Northern New Jersey. All white males between the ages of 30 and 64 years in the selected counties with a diagnosis of malignant melanoma who were first diagnosed between July 1, 1978, and December 30, 1980, will be eligible as cases. Age-sex-race population matched controls will be selected.

Information obtained from records of private dermatopathology laboratories and hospital pathologist records will be used to determine cases aided by the New Jersey, New York and Pennsylvania cancer registers. All cases will be ascertained as malignant melanoma by a board certified dermatopathologist. Home interviewing of cases and controls will obtain information on: residence history, work exposure history (particularly to chemical substances), sun exposure, history of cancer in the family and history of chloracne dermatitis.

Preliminary work has provided suggestive evidence of a large relative risk of malignant melanoma among workers exposed to polychlorinated biphenyls (PCBs) and other chemicals. New Jersey has been selected as the locale for the study because this state has the largest number of workers in chemical and related industries in the nation and because high melanoma mortality rates (for an area outside the South) have been noted among males.

Investigation will be carried out to determine if there are significant differences between cases and controls in exposure to chemical substances, exposure to sunlight, or a previous history of chloracne dermatitis.

45. MORTALITY EXPERIENCE AMONG POLYCHLORINATED BIPHENYL WORKERS

Bertazzi, P. A., Zocchetti, C., Guercilena, S., Riboldi, L., Universita degli Studi di Milano, Inst. of Occupational Health, Dept. of Epidemiology, *Via San Babila 8, 20122 Milan, Italy*

Animal experiment studies and some human data support a possible association between polychlorinated biphenyls (PCBs) exposure and cancer in man. The aim of the study is to assess mortality in the period 1955-1975 among workers employed in a capacitor and transformer industry operating since 1947. The personal records of the 2,317 workers employed since the beginning of manufacture have been obtained from the factory. For each subject date and place of birth, date of entry and leaving the industry and type of work performed are available; date, place, and primary cause of death will be ascertained from death certificates. The sex, age and cause-specific mortality of people living in the same city where the factory is located will be used for comparison.

46. MORTALITY, MEDICAL, AND INDUSTRIAL HYGIENE STUDY OF WORKERS EXPOSED TO PCBS - NCI

Smith, B., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Polychlorinated biphenyls (PCBs) are a class of chlorinated aromatic hydrocarbons that are widespread in the environment, are highly stable, and tend to bioconcentrate in the food chain. Their current use is primarily limited to close systems in the electrical industry as insulating material in capacitors and transformers. Reports of adverse health effects in humans and animals accidentally exposed to PCBs, and the demonstration of carcinogenic effects in certain animals from certain PCBs, have necessitated an evaluation of the toxicology of this class of compounds. In laboratory animals, structural function changes in the liver have been noted as well as heptic tumor induction in certain species. Other documented effects have included gastrointestinal, endocrinological, hematological and embryotoxic effects. In humans, the syndromes of chloracne, and Yusho neonatorum have been extensively documented.

A determination of the health effects from exposure to PCBs is being assessed by (1) a retrospective mortality study of a cohort of occupationally exposed workers; (2) a cross-sectional medical survey of a cohort of currently employed workers; (3) a detailed industrial hygiene survey.

The mortality study is well under way; follow-up is near completion on the two study cohorts exposed to PCBs. The medical surveys have been completed and data analysis is in progress. The industrial hygiene surveys on all plants that were included in the mortality study and medical study have been completed.

47. MALIGNANT LYMPHOMAS AND EXPOSURE TO CHEMICALS, ESPECIALLY TO PHENOXYACETIC ACIDS, CHLOROPHENOLS OR ORGANIC SOLVENTS

Hardell, O. L., Eriksson, M. H., Lenner, P., Regionsjukhuset, Dept. of Oncology, *90185 Umea, Sweden*

In 1977 a number of patients with soft tissue sarcomas and previous exposure to phenoxyacetic acids were reported in this department. This included an analysis of exposure to chlorophenols. The results showed that exposure to phenoxyacetic acids or chlorophenols gave an approximately six-fold increase in the risk for this type of tumor. In May, 1978, a patient with a tumor in the soft tissue of his left femur was admitted to this department. The clinical picture was similar to that of a soft-tissue sarcoma. Histological examination showed, however, a malignant lymphoma of histiocytic type. The patient reported a massive exposure to phenoxyacetic acids. All male patients with this type of tumor who were admitted to the department during January to September, 1978, were then asked about their past and present occupation and about possible exposure to phenoxy acids or chlorophenols. In this pilot study, 14 of 17 patients reported a current occupation which was consistent with the possibility of exposure to the chemicals under study - namely, farming or forestry (7), saw mill work (1), painting (3) and building (3). Eleven men reported exposure to phenoxyacetic acids or chlorophenols. An epidemiological study is now being performed. The cases are 173 men with malignant lymphomas, aged 25-85 years, admitted to this department in 1974-1978. For each case two controls are selected, matched by geographical region, sex and age. The chemicals under consideration are phenoxyacetic acids, chlorophenols and organic solvents.

48. CASE-CONTROL STUDY OF SOFT TISSUE SARCOMAS AND EXPOSURE TO CHEMICAL AGENTS

Eriksson, M. H., Hardell, O. L., Axelson, O., Berg, N. O., Moeller, T., Regionsjukhuset, Dept. of Oncology, *90185 Umea, Sweden*

In 1978 a matched case-control study performed in this insitution showed that exposure to phenoxyacetic acids or chlorophenols gave an approximately sixfold increase in the risk of soft tissue sarcomas. This investigation was carried out in the northernmost counties in Sweden, where forestry is common. All exposed cases except two had been in occupational contact with either chlorophenols or the phenoxyacetic acid 2,4,5-T (2,4,5-trichlorophenoxyacetic acid), which are both often associated with impurities such as chlorinated dibenzodioxins or dibenzofurans, among them the toxic 2,3,7,8-tetrachlorodibenzodioxin (TCDD). Thus it could not be decided whether the increased risk was due to the impurities or to the chemicals studied. To try to determine this, a new matched case-control study is being carried out in the agricultural area of the five southernmost counties in Sweden, since phenoxyacetic acids without the impurities mentioned above are extensively used in farming. The cases in this new study are 110 men, aged 25-75, with soft tissue sarcomas diagnosed between 1974 and 1978 in the region studied. For each case two controls are selected, matched by geographical district, sex and age.

49. INVESTIGATION OF PENTACHLOROPHENOL AND CANCER RISK

Aldrich, T. E., Duncan, R. C., University of Miami, School of Medicine, Dept. of Epidemiology & Public Health, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida*, 33152, United States of America

This study began as an investigation of citizen-reported clustering of cancer, associated with possible pentachlorophenol (PCP) exposure. Suggestive findings from this field study prompted a larger, non-current, prospective study of occupational exposure to PCP to quantify any associated cancer risk. An anticipated 1,000 persons will be included in the study, and a control group will be selected form a non-related industry.

50. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF PCE WORKERS - NCI

Brown, D., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Surveillance, Hazard Evaluations & Field Studies Division, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Perchloroethylene (PCE) is used extensively throughout the dry cleaning industry (100,000 workers). PCE has been tested for carcinogenicity in the Bioassay Program of the National Cancer Institute. The results of this experiment were similar to those seen with trichloroethylene - that is, an increase in hepatocellular carcinomas in mice. To date, the effects on humans from long-term low level exposure to PCE is unknown.

This study will assess the health effects from exposure to PCE by analysis of cause specific mortality among an identified group of dry cleaning workers. A cause of death for each individual in the cohort will be determined retrospectively and the observed deaths will be compared to those expected based on a standard race-, sex-, and age-specific population. Industrial hygiene surveys will be conducted by NIOSH to characterize worker exposure to PCE in the dry cleaning industry.

The Stanford Research Institute (SRI) is conducting the mortality study under contract. Personnel records from four labor unions have been used to assemble a cohort of approximately 1,650 dry cleaning workers who were employed for at least one year prior to 1960 in a facility where the primary solvent was perchloroethylene. All of the demographic and work history coding has been completed and vital status follow-up through the Social Security Administration has been accomplished. Once the SSA data is processed it will be determined how much more vital status follow-up is necessary.

Industrial hygiene surveys have been conducted in 30 dry cleaning facilities in San Francisco-Oakland, Detroit, and Cincinnati. An additional 15-20 surveys are planned in New York City and Chicago. The final I.H. report will be furnished in early FY 80.

51. RETROSPECTIVE COHORT MORTALITY STUDY OF DRY CLEANING WORKERS EXPOSED TO PERCHLOROETHYLENE

Kaplan, S. D., Brown, D. P., SRI International, Center for Occupational & Environmental Safety & Health, *333 Ravenswood Ave., Menlo Park, California*, 94025, United States of America

Perchloroethylene is a principal solvent in the dry cleaning industry. This chlorinated hydrocarbon has been shown to cause liver cancer in one strain of mice but not in one strain of rats. The objectives of the study are to identify a population of at least 2,000 individuals in dry cleaning facilities exposed to perchloroethylene as a primary solvent and not previously exposed occupationally to either trichloroethylene or carbon tetrachloride who were employed for at least 12 months before 1960, obtain sufficient data to make possible calculation of expected mortality as a function of exposure, carry out a follow-up, obtain death certificates and analyze and interpret the results. Eligibles for the cohort have been identified from four union locals, supplemented by solvent histories from sources including: equipment manufacturers and distributors, solvent distributors, and industry representatives. Follow-up will be through the Social Security Administration supplemented as needed by Motor Vehicle Registration and the Tel-Credit Bureaus. A modified life table analysis will be performed.

52. TETRACHLOROETHANE EXPOSURE AND SUBSEQUENT MORTALITY FROM CANCER IN U.S. ARMY VETERANS OF WORLD WAR II

Norman, J., Robinette, C. D., Fraumeni, J. F., National Academy of Sciences, National Research Council, Medical Follow-Up Agency, *2101 Constitution Ave. N.W., Washington, District of Columbia*, 20418, United States of America

Heavy exposures to chemical hydrocarbons in man result mostly from industrial chemicals and pesticides, but most exposures are recent and do not lend themselves to epidemiological investigation. One member of this class of compounds, tetrachloroethane, has had wide industrial use and was also used by the Army during World War II in the impregnation of clothing against mustard gas. One-fourth of the 39 Army Chemical Processing Companies used tetrachloroethane as a solvent in the impregnation process while the remainder used an improved process in which water replaced this compound. Cases and controls are thus defined on the basis of company assignment and military speciality. The mortality experience of some 13,300 men (cases and controls) is being studied to determine the effect of exposure to the chemical on cancer mortality.

53. MORTALITY AND MORBIDITY SURVEY OF THE OCCUPATIONAL RISK OF DIMETHYLCARBAMAZINE-CHLORIDE (ABBREV)

Thiess, A. M., Frentzel Beyme, R. R., Hey, W., Badische Analin & Soda Fabrik Ag, Werksaerztliche Abteilung, *Brunckstrasse 56, 6700 Ludwigshafen, Federal Republic of Germany*

DIMCA (dimethylcarbamylchloride) ((CH3)2 NCOCl) has been described as a multipotential carcinogen to ICR/Ha Swiss mice by application to skin and subcutis. After one year on test, a 68% incidence of tumours (46% papillomas and 22% carcinomas) resulted from application and 72% incidence of local sarcomas by subcutaneous injection. Another localization was lung tissue, though with comparatively low incidences (4-8%, compared to 0% in untreated controls). DIMCA is considered a directly acting alkylating carcinogen. The study is designed to assess the total continuously exposed work force in the production of DIMCA in order to investigate cancer incidence as suggested by carcinogenic effects in animal experiments.

54. RESPIRATORY EFFECTS OF CHLOROMETHYL ETHERS

Weiss, W., Hahnemann Medical College & Hospital, Medical College, Dept. of Medicine, *235 N. 15th St., Philadelphia, Pennsylvania*, 19102, United States of America

A prospective study of 125 male workers at a chemical plant by periodic chest x-rays and questionnaires was conducted from 1963 to 1968. In 1965 a spirogram was done in 103 men. Additional follow-up has been continued to the present. Ninety-one men had been exposed to the chloromethyl methyl ether containing bis (chloromethyl) ether as a contaminant. Each man was assigned an exposure index obtained by multiplying a semi-quantitative time-weighted average exposure rating against the years of exposure. The men were divided into an unexposed and three exposed groups according to the magnitude of the index. The groups were similar except that the most heavily exposed group had more non-smokers and more light current cigarette smokers than the other groups. There was a dose-response relationship between chemical exposure and the prevalence of chronic cough and expectoration, and the 10 year incidence of bronchogenic carcinoma with no cases among lightly exposed men and increasing risk in moderately and heavily exposed men. Although the groups did not differ with respect to the frequency of abnormal forced vital capacity and forced expiratory volume in one second, there was a rough relationship between the degree of chemical exposure and the frequency of low end-expiratory flow rate on the spirogram. There was an inverse relationship between smoking habits and the risk of lung cancer. All of the cancers were small cell in type. Observation of the cohort is continuing.

55. MORTALITY STUDY OF OCCUPATIONAL EXPOSURE TO HALO ETHERS

Pasternack, B. S., Shore, R. E., Albert, R. E., Lippmann, M., New York University, School of Medicine, Dept. of Environmental Medicine, *100 Washington Sq. E., New York, New York*, 10003, United States of America

Chloromethyl-methyl ether (CMME) and his-chloromethyl ether, an impurity (2-8%) in commercial CMME, are alkylating agents having diverse use in the chemical industry. Animal studies have demonstrated that both compounds are potent lung carcinogens. A retrospective cohort study of occupational exposure to CMME was initiated in 1972 to evaluate the human carcinogenicity of these compounds. The initial survey showed a clear excess of respiratory cancer among the CMME-exposed

workers, and a strong exposure-response relationship. Other findings among the exposed workers were a considerable number of respiratory cancers at early ages (before age 45), an excess among both smokers and non-smokers, and an inverse relationship between dose and respiratory cancer latency. Particularly because of the latter finding, another mortality survey is underway to better characterize the risk for those with lower exposure levels. The survey will include all seven major CMME producer and user firms in the USA for the time period 1948-1979. An estimated 2,000 CMME-exposed workers and 3,500 unexposed workers will be available for study.

56. CHLOROMETHYL-METHYL ETHER STUDY

McCallum, R. I., Petrie, A., University of Newcastle upon Tyne, Dept. of Occupational Health & Hygiene, *6 Kensington Terr., Newcastle upon Tyne NE1 7RU, England, United Kingdom*

The aim is to determine whether workers in two factories manufacturing chloromethyl methyl ether in United Kingdom have an excess lung and nasal cancer mortality.

57. MORBIDITY AND MORTALITY STUDY OF BENZOTRICHLORIDE WORKERS

Cooke, M. A., Waterhouse, J. A., Albright & Wilson Ltd., Dept. of Medicine, *P.O. Box 80, Oldbury B69 4LN, England, United Kingdom*

OBJECTIVE: To assess incidence of respiratory and other neoplasms in benzotrichloride workers in view of the published work of Sakabe.

3. OTHER ORGANIC CHEMICALS

58. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF WORKERS EXPOSED TO DYES

Haring, M., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

In response to concern about the carcinogenicity of chemical components of oxidative and 'coal tar' hair dyes, the possibility of investigating the mortality experience of cosmetologists has been reviewed; an extensive review of records from state licensing bureaus and national cosmetologist organizations found the available data inadequate to conduct a comprehensive epidemiological or industrial hygiene study of cosmetologists as an occupational group. Another occupational group exposed to oxidative dyes includes animal fur dyers, who have been using phenylenediamine (used as an intermediate in hair dyes) in their dyeing processes since the turn of the century. Therefore, the Industry-wide Studies Branch has undertaken jointly with the National Cancer Inst. a retrospective cohort mortality study of fur dyers in the New York City area. The records of the Joint Board of the Fur, Leather and Machinists Workers' Union (FLM) have been chosen as the principal data source. Due to the restricted nature of the records, the study was limited to retirees (pensioners) on whom the most complete documentation was kept. Follow-up for the cohort is continuing, mainly through the Social Security Administration. A second union, local 3 of the Fur Floor Workers' Union, has been contacted for possible inclusion in the study. This is an excellent data source for a mortality study of all workers including active, terminated and retirees. Their data on retirees could be used to supplement those of the FLM due to the similarities in ethnic background, geographical location of the shops and jobs performed.

59. MEDICAL SURVEILLANCE AND INTERVENTION - BLADDER CANCER

Bayliss, D. L., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

As aromatic amines, specifically beta-naphthylamine, benzidine, and di-chloro-benzidine, have been responsible for cancer of the bladder in up to 100 percent of workers, the continued and increasing use of such carcinogens, not only in dye and pigment production but also in pharmaceuticals, detergents, food colors and specialized chemicals, makes it imperative that surveillance should continue so that situations similar to the current bladder cancer epidemic in New Jersey be prevented. A cooperative agreement is being developed with the National Cancer Institute to place all such exposed workers under medical surveillance. This will include periodic examinations and constant follow-up to detect early changes consistent with the development of bladder cancer.

60. CYTOLOGICAL MONITORING OF WORKERS EXPOSED TO AROMATIC AMINES IN A SYNTHETIC DYES PLANT

Melinte, L., Barhad, B., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Medicine, Cytopathology, *Strada Biserica Amzei 29, Bucharest, Romania*

Biennial cytological screening, together with wet urinary sediment examination and the urological control (cystoscopy), has been conducted since 1970 to study the effect of occupation on urinary bladder cancer. The results are correlated with age, sex, smoking habits, length of exposure and exposure levels. The cases discovered in the early phase have a high survival rate.

61. MEDICAL, INDUSTRIAL HYGIENE, AND REPRODUCTIVE STUDIES OF WORKERS EXPOSED TO ESTROGENS

Tanaka, S., Zaebst, D., Haring, M., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Estrogens are a group of synthetic and natural hormones having serious potential effects on exposed workers. NIOSH hazard evaluation studies which were carried out in chemical and pharmaceutical manufacturing plants indicated that male workers developed gynecomastia and female workers experienced intermenstrual bleeding. It has been documented that women taking oral contraceptives have an increased risk of thromboembolism, cerebral vascular disease, and myocardial infarction. It has also been noted that estrogens may be carcinogens (e.g., increased incidence of endometrial cancer among women on estrogen replacement therapy. DES is a transplacental carcinogen/teratogen to the offsprings).

A cross-sectional medical/industrial hygiene study has been initiated to study health problems of workers exposed to estrogens and to attempt to determine a safe level of exposure to these agents. During the second quarter of FY 78, a workshop was held (in lieu of the tripartite meeting) which was attended by representatives of the pharmaceutical manufacturing plants and a substantial amount of information was collected on manufacturing processes, employee profiles, etc. Five of these plants were selected for in-depth study; four of these manufacture oral contraceptives using synthetic estrogens and one proccesses conjugated estrogens of natural origin. It was also determined that there is no longer a plant in the U.S. which chemically manufactures DES in bulk and that pharmaceutical preparations containing DES are manufactured only sporadically. Because of this, it was decided that occupational effects of DES exposure will not be studied in this project. Feasibility determinations regarding the mortality study of workers occupationally exposed to products containing estrogens have been completed in all but one plant. The remaining company has been contacted and a walk-through survey date is being negotiated.

62. MORTALITY, MEDICAL AND INDUSTRIAL HYGIENE STUDIES OF WORKERS EXPOSED TO SYNTHETIC ESTROGENS

Selevan, S. G., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Synthetic estrogens are a group of synthetic hormones having serious potential effects on exposed workers. Women taking oral contraceptives have an increased risk of thromboembolism, cerebral vascular disease, and myocardial infarction. A study by the National Institute for Occupational Safety and Health (NIOSH) carried out in an oral contraceptive plant indicated that problems are occurring in both males (gynecomastia) and females (menstrual changes). Also, it has been noted that estrogens may be carcinogenic. A cross-sectional medical/environmental study is proposed to investigate health problems re-

sulting from exposure to synthetic estrogens and to attempt to determine a safe level of exposure to these agents. A mortality study of workers occupationally exposed to oral contraceptives will be performed to determine if an excess number of carcinoma deaths have occurred in exposed workers.

63. HUMAN HEALTH CONSEQUENCES OF POLYBROMINATED BIPHENYLS (PBBS) CONTAMINATION OF FARMS IN MICHIGAN

Heath, C. W., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, *1600 Clifton Rd. N.E., Atlanta, Georgia*, 30333, United States of America

OBJECTIVE: As a consequence of the distribution of animal feeds contaminated with PBB, the inhabitants of at least 412 Michigan farms as well as a wide surrounding belt of consumers, were accidentally exposed to that potentially threatening compound. This activity defines and recruits large cohorts of individuals (of several degrees of exposure) and will engage in a long-term follow-up primarily with respect to the incidence of cancer.

MAJOR FINDINGS: The major effort to date has been the development of cohorts. Two blood samples have been taken from all PBB exposed individuals and analyzed for this compound as well as for polychlorinated biphenyls (PCBs); this is of equal interest scientifically and provides gratuitous information. Certain high risk groups (high blood level individuals engaged in the production of the PBB compound and children born during or after the incident) continue to be monitored closely. The initial scientific impression that there were little or no immediate or acute effects on the subject population appears to have been verified.

SIGNIFICANCE TO BIOMEDICAL RESEARCH AND PROGRAM OF THE INSTITUTE: This is a unique situation in which a large group of people had a known exposure to a potential carcinogen under sharply defined circumstances of geography and time. Unfortunate subsequent rises in cancer incidence, if they occur, can thus be charted in this prospective study and correlated with modes and amount of exposure. Major scientific observations on this particular compound and structurally allied compounds can be developed.

PROPOSED COURSE: Cohorts having been defined and recruited, the major effort for the foreseeable future is to maintain their integrity for the long-term determinations. Deaths, illness, pregnancies, etc., will be carefully monitored. It is anticipated that the scaling down of effort will continue to some degree because of the completion of major tasks.

64. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF WORKERS EXPOSED TO STYRENE - NCI

Beaumont, J., Crandal, L., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Recently, information has evolved which indicates that workers exposed to styrene may experience chronic health problems: (1) There have been studies which show a definite increase in deaths due to leukemia among styrene-butadiene rubber workers. (2) Styrene has been shown to be mutagenic after liver microsomal activation. (3) Styrene oxide, which is a metabolite of styrene, has been shown to be mutagenic by the Ames test. Hepatotoxicity and carcinogenicity have been attributed to chronic exposure to styrene metabolites based on animal experiments. As a result of this information, a retrospective mortality study and industrial hygiene study of workers exposed to styrene is being conducted to further evaluate the potential medical effects of styrene.

Preliminary industrial hygiene and record assessment evaluations have been conducted at fifteen boat manufacturing facilities, both in and outside of the State of Washington, in order to judge the feasibility for their inclusion in the epidemiologic study. Two of these facilities in the State of Washington were identified as appropriate for the mortality study. In addition, five other facilities were chosen for industrial hygiene monitoring alone. A total of seven industrial hygiene surveys were carried out.

Demographic files have been coded and are being verified for the retrospective mortality study. Vital status follow-up has begun for all individuals who have worked at the two facilities which are part of the epidemiologic study.

65. MORTALITY EXPERIENCE OF STYRENE WORKERS

Zack, J. A., Monsanto Co., Dept. of Medicine & Environmental Health, *800 N. Linbergh Blvd., St. Louis, Missouri*, 63141, United States of America

Employees from several plant locations who have been exposed to styrene are being identified for study. The cohort will be traced prospectively and their mortality experience will be evaluated using the standardized mortality method. Particular attention will be given to deaths from malignant neoplasms and from neoplasms of lymphatic and hematopoietic tissue.

66. EPIDEMIOLOGICAL STUDY OF BENZENE EXPOSED WORKERS

Weaver, N. K., Irving, R., Tabershaw, M. D., American Petroleum Inst., Dept. of Medicine & Biological Science, *2101 L St. N.W., Washington, District of Columbia*, 20037, United States of America

The objective of the study is to determine the mortality rates of workers exposed to benzene in petroleum operations. Workers having known exposures to benzene will be identified, and their mortality rates determined and compared with those of other groups. Secondary studies will include proportionate mortality from pooled company records; a study of effects on health, particularly blood counts, as they relate to benzene exposure; development of a job title dictionary for exposure dosage; and establishment of a prospective medical mortality and environmental study. If primary studies reveal excess mortality from specific diseases, especially leukaemia, latency periods, dose relationships and host factors will be studied.

67. LEUKEMIA INCIDENCE AMONG WORKERS EXPOSED TO BENZENE

Aksoy, M. B., Erdem, S., Dincol, G., Istanbul Universitesi, Faculty of Medicine, Section of Hematology, *Bayezit, Istanbul, Turkey*

Further follow-up of persons in work places where aplastic anemia and leukemia associated with benzene exposure occurs, continues. During the period 1967-1969 44 cases of leukemia were noted in addition to nine patients with malignant lymphoma, five with carcinoma of lung, three with multiple myeloma, three with myeloid metaplasia and two with paroxysmal nocturnal hemoglobinuria.

68. EPIDEMIOLOGICAL STUDY OF WORKERS EXPOSED TO BENZENE

O'Berg, M. T., E.I. du Pont de Nemours & Co. Inc., Medical Division, *1007 Market St., Wilmington, Delaware*, 19898, United States of America

This is a retrospective cohort study of 2,000 workers exposed to benzene at some time between 1910 and 1976. Follow-up of terminated employees will be undertaken and mortality experience of the entire cohort will be compared with expectation based on the entire du Pont Company workforce, and on the US population. Particular attention will be given to cancer, especially leukemia.

69. MORTALITY STUDY OF UK ACRYLONITRILE WORKERS

Duncan, K. P., Werner, J. B., Jones, R. D., Health & Safety Center, *97 Horseferry Rd., London SW1P 2DY, England, United Kingdom*

The study takes the form of an examination of the mortality pattern of 1,300 acrylonitrile polymerization process workers who were first exposed to acrylonitrile in 1968 or earlier in six factories in the UK. Data on job histories and exposure levels will be used to allocate workers to defined exposure groups. Mortality from all causes of death, together with selected causes including cancer of lung, brain and large intestine, will be considered.

70. MORTALITY EXPERIENCE OF ACRYLONITRILE-EXPOSED WORKERS

Zack, J. A., Monsanto Co., Dept. of Medicine & Environmental Health, *800 N. Linbergh Blvd., St. Louis, Missouri*, 63141, United States of America

This is a mortality study of workers exposed to acrylonitrile through its manufacture and use. Approximately 400 wage

employees from two plants have been identified for study. The mortality experience of these workers will be analyzed by the standardized mortality method, with particular attention given to malignant neoplasms of the lung and colon.

71. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF WORKERS EXPOSED TO TETRAETHYL LEAD

Haring, M., Crandall, M., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Preliminary epidemiologic investigation of employees of one company involved in the production of tetraethyl lead has revealed three cases of multiple myeloma, two living and one deceased. These three cases represent approximately 30 times the rate expected. More comprehensive case ascertainment is being proposed to locate other diagnosed cases, both living and dead, in the same workforce. This will be accomplished by expanding a continuing retrospective cohort mortality study conducted by the company and by mailing questionnaires to former and current employees. Dependent on the results of more extensive case findings, it is proposed to screen the population for asymptomatic multiple myeloma. Multiple myeloma often demonstrates a lengthy course prior to diagnosis. The cost of laboratory tests might range from 40 to 70 dollars per person.

The industrial hygiene portion of this project will include both preliminary and in-depth characterizations of the work environment in the tetraethyl lead production areas. Personal and area monitoring for tetraethyl lead, the reactants in the production process, and other additives used in the blending operations will be included.

72. A MORTALITY STUDY OF PEST CONTROL OFFICERS

Thomas, H. F., Medical Research Council, Epidemiology Unit, *4 Richmond Rd., Cardiff CF2 3AS, Wales, United Kingdom*

A pilot study is being conducted to examine the feasibility of obtaining information from local authorities in England and Wales on pest officers employed from 1946 onwards, and on the pesticides used. A special interest is being taken in the use of 'antu' (alpha-naphthylthiourea), a rodenticide which chemical tests suggested could be associated with bladder cancer, and which was generally withdrawn from use in the UK in 1967. Commercial pest control firms are also being contacted and some may cooperate in a retrospective study; the feasibility and value of prospective studies will also be considered.

73. HEALTH EFFECTS DUE TO AN ACCIDENTAL EXPOSURE TO DIMETHOATE

Matos, E. L., Urquijo, C., Instituto Oncologia Angel H. Roffo, Departamento de Investigaciones, *Av. San Martin 5481, 1417 Buenos Aires, Argentina*

OBJECTIVE: In May 1979, an exothermic reaction occurred in the production of dimethoate (RN 60-51-5). The resulting escape of gases lasted 4 hours and ceased only upon consumption of all the existing product. Two persons died, and 30 exhibited symptoms of poisoning. Results of the testing of dimethoate for carcinogenicity in rats have been contradictory. On the other hand, this pesticide has been found to be mutagenic in S. cerevisiae and E. coli. The population that was most exposed, the firemen and security personnel personnel who remained on duty during the entire fire, as well as the nearby neighbors, will be studied.

METHOD: Chromosomes of the peripheral lymphocytes of those firemen who remained on the spot and exhibited symptoms of poisoning are under study. Currently, efforts are being made to contact all exposed persons. They will be followed-up and controlled every 6 months.

74. MORTALITY AND MORBIDITY SURVEY OF OCCUPATIONAL RISK OF ETHYLENE AND PROPYLENE OXIDE IN CHEMICAL PRODUCTION AT BASF, LUDWIGSHAFEN, GERMANY

Thiess, A. M., Frentzel Beyme, R. R., Link, R., Stocker, W., Badische Analin & Soda Fabrik Ag, Abt fuer Arbeitsmedizin und Gesundheitsschutz, *Bruncksstrasse 56, 6700 Ludwigshafen, Federal Republic of Germany*

Ethylene oxide (EO) is known to be a mutagen in various biological systems like bacterias, animal and human tissues. This led to a suspicion that EO might be a potential carcinogenic risk. A cohort study was designed to assess cancer incidence in those occupational groups which have been exposed to both ethylene and propylene oxide. The chemical workers ever exposed to the substance are followed up for mortality experience (cause of death) and for morbidity. The follow-up includes careful tracing of retired and resigned persons. The problem of possible mixed exposure has to be taken into consideration.

75. MORTALITY AND MORBIDITY SURVEY OF THE OCCUPATIONAL RISK OF ETHYLENE-IMINE

Thiess, A. M., Frentzel Beyme, R. R., Link, R., Tress, M. D., Badische Analin & Soda Fabrik Ag, Werksaerztliche Abteilung, *Bruncksstrasse 56, 6700 Ludwigshafen, Federal Republic of Germany*

This study is to assess cancer incidence in occupational risk groups as suggested by carcinogenic effects of ethylene-imine observed in animal experiments. The chemical workers overexposed to the substance are followed up for mortality experience (cause of death) and for morbidity (as far as data are available). The follow-up includes careful tracing of persons who either retired or resigned.

76. MORTALITY AND MORBIDITY SURVEY OF THE OCCUPATIONAL RISK OF DIMETHYLSULFATE (AS A POTENTIALLY CARCINOGENIC SUBSTANCE)

Thiess, A. M., Frentzel Beyme, R. R., Badische Analin & Soda Fabrik Ag, Werksaerztliche Abteilung, *Bruncksstrasse 56, 6700 Ludwigshafen, Federal Republic of Germany*

The study is to assess cancer incidence in occupational risk groups as suggested by carcinogenic effects of dimethylsulfate observed in animal experiments. The chemical workers overexposed to the substance are followed up for mortality experience (cause of death) and for morbidity (as far as data are available). The follow-up includes careful tracing of retired and resigned persons.

77. COHORT MORTALITY STUDY OF DIMETHYLNITROSAMINE WORKERS

Nicholson, W. J., City University of New York, Mount Sinai School of Medicine, Dept. of Community Medicine, *1 Gustave L. Levy Pl., New York, New York*, 10029, United States of America

This proposed research will establish a cohort of workers exposed occupationally in the past to dimethylnitrosamine. Prospective observation of their full mortality experience, from the time of first exposure, will be conducted. Expected and observed rates of death by cause will be tabulated to ascertain if unusual mortality patterns exist. Such data will have importance in assessing the potential human carcinogenicity of dimethylnitrosamine and in assessing the potential risk of environmental exposure of N-nitroso compounds.

78. MORTALITY STUDY OF DIESEL ENGINE MECHANICS

Costello, J., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Respiratory Disease Studies, *944 Chestnut Ridge Rd., Morgantown, West Virginia*, 26505, United States of America

A few years ago a suggestion was made to introduce diesel powered equipment into underground coal mines to replace electrically operated equipment. Labor unions expressed concern about this in terms of both health and safety. NIOSH held a conference in September, 1977, to determine what was known about health effects of diesel exhaust. One recommendation of this conference was for NIOSH to look at a large population of workers who had been exposed to diesel exhaust in confined spaces for an extended period of time.

Diesel engines have been found to emit polynuclear aromatic hydrocarbons. Among these emitted polynuclear aromatic hydrocarbons are found benzo(a)pyrene (B(a)P) and benz(a)anthracene (B(a)A) which are known to be carcinogenic. Work by Carnow and others suggests that an increase of 1 mg/cu.m B(a)P in urban pollution is associated with a 5% increase in lung cancer death rate. Battigelli and others in 1963 looked at 210 workmen exposed to diesel exhaust in railroad engine

houses and found that there was no significant difference in pulmonary function between these workers and a control group. However, the maximum latent period was 15 years with an average of 10-year exposure and the study group was small.

Railroads began dieselization in earnest after the Second World War and by 1953 were well on the way toward complete dieselization. We now have a maximum latent period of 24-plus years which should be long enough to show evidence of lung cancer, if it exists, in these workers. This project will look at mortality patterns of a large group of workers in railroad diesel engine repair shops (and other diesel repair shops) where it is common practice for engines to be left running for adjustments. Particularly in inclement weather the shop doors are closed and inadequate ventilation may result. We will pick a sample of the larger shops in the eastern United States for this project.

79. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF ALUMINUM REDUCTION WORKERS

Brown, D., Bloom, T., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Workers in the aluminum reduction industry are exposed to a variety of substances: hydrogen fluoride fumes, dust, carbon monoxide and coal tar pitch volatiles (CTPV) such as benz(a)pyrene. Coal tar pitch volatiles are released in the anode preparation area in plants using pre-baked anodes and in the pot lines where Soderberg self-baking cells are used. The release of CTPV is thought to be temperature dependent. Sufficiently high temperatures are reached in both anode preparation and electrolysis of aluminum to achieve the release of such materials. Thus, there is concern for the health of aluminum workers who may be exposed to carcinogens within CTPV such as B(a)P. Industrial hygiene surveys of the aluminum reduction industry have revealed levels of coal tar pitch volatiles well above the current occupational health standard of 0.2 milligram per cubic meter (mg/cu.m) by the benzene soluble fraction method. A variety of studies have been carried out to describe the cancer mortality experience of workers in aluminum reduction facilities.

In order to more fully define the specific cancer risk within the industry, a retrospective case/control study is being carried out on aluminum reduction workers. Industrial hygiene will assist in classifying job categories and in verifying related industrial hygiene data. The case-control study will use existing data generated from a previous study. The cases and controls have been selected, the work histories have been coded, and some preliminary analyses have been run. Environmental measurements are being calculated for the various job titles included in the case-control study, so that the analysis can take full advantage of exposure-response data.

80. ANALYSIS OF MORTALITY PATTERNS IN ALUMINUM REDUCTION PLANTS

Rockette, H. E., University of Pittsburgh, Graduate School of Public Health, Dept. of Biostatistics, *4200 5th Ave., Pittsburgh, Pennsylvania*, 15260, United States of America

A review of the literature on the health effects of worker exposures in the reduction of aluminum indicates that there may be an excessive incidence of respiratory cancers among workers exposed to high levels of coal pitch volatiles. Furthermore, there may be an excessive incidence of other cancers and of chronic obstructive respiratory disease. The largest study to date was a historical prospective study sponsored by the Aluminum Association. In that study, 23,033 men employed for five years or more during the period 1941-1973 at one of fifteen aluminum reduction plants in the United States were followed up through 1973. The present study will use these records as a data base. The objectives of the new study are as follows: (1) to verify the accuracy of the initial data collection, (2) to obtain job histories and include these in the analysis, (3) to obtain estimates of exposure levels, and (4) to extend the follow-up period through 1977. Mortality patterns of groups of workers with varying levels of exposure and of general populations will be compared.

81. LUNG CANCER MORTALITY IN ALUMINUM REDUCTION WORKERS

Gibbs, G. W., McGill University, Inst. for Mineral Industry Research, Occupational Health & Safety Unit, *Gault Estate, Mont St. Hilaire, Quebec*, J3G 4S6, Canada

The study aims to determine the lung cancer mortality of workers in three aluminum reduction plants for the 4 year period 1 January 1974 to 31 December 1977 and to examine the relationship between lung cancer mortality and length of employment and level of tar exposure. The methods to be applied are identical to those in an earlier study of lung cancer mortality (1950-1973) currently in press. The populations under study consist of 2 cohorts employed at aluminum reduction plants, one of 5,406 workers who were working at plant A on 1 January 1950 and the other of 485 workers who were working at plant B on 1 January 1951. The mortality experience from lung cancer for this population was studied to 31 December 1973. The period of observation will now be extended to 31 December 1977. The pattern of mortality for the 2 periods 1950-1973 and 1974-1977 will be examined to determine any change in the relationships between lung cancer mortality and tar exposure.

82. CAUSES OF MORTALITY AND DISABILITY IN FERRO-ALLOY WORKERS

Pokrovskaya, L. V., Sverdlovsk Research Inst. of Hygiene of Labor & Occup. Dis., Dept. of Industrial Hygiene, *Repin 2, Sverdlovsk 620014, Russia, Union of Soviet Soc. Republics*

Previous work has shown that the mortality from cancer in workers handling chrome-containing ferro-alloys is significantly higher than in the general population. These workers had a heavy exposure not only to chrome compounds but also to polycyclic aromatic hydrocarbons (PAH), especially benz(a)pyrene. The present study aims to explore the causes of death and disability among smelters of various ferro-alloys (exposed not to chrome but to PAH), particularly from malignant lymphoma and leukaemia. The follow-up of the cohort began in 1955 and continued until 1974.

83. MORTALITY STUDY OF SYNTHETIC GRAPHITE ELECTRODE MANUFACTURING WORKERS

Nakamura, K., Sakabe, H., National Inst. of Industrial Health, Dept. of Industrial Epidemiology, *2051 Kizuki Sumiyosityo, Kawasaki, Kanagawa, Japan*

Studies of mortality among coke oven workers indicate that the excess of respiratory cancer is related to exposure to coal tar effluents. In the production of synthetic graphite electrodes, coal tar pitch is used as a binder for cokes (petroleum and coal). A cohort study has been carried out for the 5,025 workers who had or have been employed in all 14 electrode manufacturing plants in Japan. For the retired and employees who have left the industry, ascertainment of death is obtained from the family registry system in Japan and death certificate information is collected from the District Legal Affairs Bureau. By the end of 1974, 63 deaths from malignant neoplasms had occurred in the cohort, including 7 respiratory cancers. Follow-up continues prospectively.

84. HEALTH EFFECTS OF THE PETROCHEMICAL INDUSTRY

Glazer, E. R., Harris, J. A., Nelson, V. E., Reed, D. M., Goldsmith, J. R., Austin, D. F., Deane, M., State Epidemiological Studies Lab., *2151 Berkeley Way, Berkeley, California*, 94704, United States of America

The refining, transportation and secondary processing of petroleum generates certain compounds known to be carcinogenic or otherwise hazardous to human health. The objective of this project is to assess the long term health effect of the petrochemical industry on workers in the industry and on the surrounding community. The initial phase of the project is being performed in Contra Costa County, California, which has four large petroleum refineries and numerous chemical plants concentrated along its northern border. Among the studies being done is a correlational analysis of measures of petrochemical emissions and health outcomes such as cancer incidence. A case-control study of childhood cancer is being planned. This will explore the relationship between parental exposure to petrochemical and the development of cancer in children and young people between the ages of 0 and 24.

85. COHORT STUDY OF REFINERY WORKERS

Puntoni, R., Vercelli, M., Valerio, F., Quintavalla, P., Santi, L. I., Universita degli Studi di Genova, Inst. de Oncologia, Dept. of Epidemiology, *Viale Benedetto 15, Pad. B, 16132 Genoa, Italy*

In the town of La Spezia there is a big refinery. The workers, approximately 500, at this refinery are exposed to several petroleum derivates. Many of these chemicals are well-known carcinogens, for instance polycyclic hydrocarbons. An investigation into the causes of death of those workers is being carried out and data on all the causes of death in the period 1960 to 1977 compiled. For comparison, the expected number of deaths will be estimated from age-specific male death rates for the La Spezia population during the same period.

86. ENVIRONMENTAL, PERSONAL AND SOCIO-ECONOMIC FACTORS IN HEMATOPOIETIC SYSTEM NEOPLASMS (HSN)

Quiroga Micheo, E., Calcagno, E. J., Calabria, S. I., Pavlovsky, S., Magnasco, J. H., Sackmann Muriel, F., Accame, E. A., Barros, C., Precerutti, A. S., De Rudoy, S. D., De Soto, Z., Grupo Argentino Cooperativo de Estudios Epid. en Hematologia, *Las Heras 1895, 1127 Buenos Aires, Argentina*

In a descriptive epidemiological study carried out in Argentina, high rates and clusters of lymphomas and multiple myeloma in zones with arsenical water were observed. A case-control study carried out on 603 case-control pairs shows: (1) no differences with regard to personal contact with cancer or HSN patients, (2) higher occupational exposure to petroleum and its products, particularly in cases of acute non-lymphocytic leukemia, (3) a greater exposure to petroleum (especially in myeloproliferative disorders and Hodgkin's disease) and insecticides (especially in acute leukemia and myeloproliferative disorders) in cases, (4) cases living in the Greater Buenos Aires area had more dogs and other animals in their homes; (5) more cases, in particular acute lymphocytic leukemias, had a simian or Sidney fold. (No differences were observed in other personal factors: mongolism, congenital abnormalities, thymoma, neoplasms, allergy, tonsillectomy, appendectomy, tuberculosis, syphilis, brucellosis, BCG, chloramphenicol, phenylbutazone, number of X-rays, etc.); (6) the socio-economic stratification was similar in both groups. This study will be extended with the aim of measuring the degree of exposure to environmental factors. A cohort study to compare the incidence of hematopoietic system neoplasms in occupations connected with exposure to petroleum with that of non-exposed persons is planned.

87. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF FUEL MEN

Halperin, W., Lemen, McCammon, U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

Workers who load jet fuel (kerosene) into commercial aircraft at JFK Airport in New York are exposed to kerosene, carbon monoxide from vehicular exhaust and aircraft exhaust, which includes a gemische of aliphatic and aromatic hydrocarbons. A preliminary investigation in response to an HHE alleging unusual death rates has uncovered several findings: 1) two of 31 deaths are due to multiple myeloma which represents an unusual fraction, and 2) maintenance and design of vehicles may allow excessive exposure to carbon monoxide. A cohort mortality study with industrial hygiene characterization of the worksite is planned.

88. BLADDER CANCER MORTALITY IN HUDDERSFIELD, YORKSHIRE

Davies, J. M., Inst. of Cancer Research, Division of Epidemiology, *Clifton Ave., Sutton SM2 5PX, England, United Kingdom*

Huddersfield is a center for the manufacture of dyestuffs, and cases of occupational bladder cancer have occurred. This study will assess the impact of occupational cases on male bladder cancer death rates in the whole town and in subdivisions since the 1930s and will assess whether the town's raised male death rates can be attributed solely to past exposure in dyestuff manufacture and will check whether bladder cancer mortaity among women is normal.

89. LUNG DISEASE (INCLUDING BRONCHIAL CARCINOMA) INDUCED BY INDUSTRIAL CUTTING OILS

Thony, C. C., Bonnavion, J., Centre de Medecine du Travail, *20 rue du Pre Benevix, Cluses, France*

In a study of lung morbidity, 100 persons with a high level of exposure to industrial cutting oils are studied. Methods include a questionnaire (adapted from the European Coal and Steel Community), clinical examination, ECG and assessment of respiratory function. 100 non-exposed persons are used as controls.

90. POSSIBLE CARCINOGENIC HAZARDS OF HAIR DYE USAGE

Crombie, I. K., Waterhouse, J. A., Searle, C. E., Regional Cancer Registry, *c/o Queen Elizabeth Med. Ctr., Birminghan B15 2TH, England, United Kingdom*

The present project is a feasibility study to determine whether a larger scale investigation could usefully be undertaken. One source of data is by questionnaire to volunteers to record their pattern of usage and to form an index file for linkage with health and mortality records. The second source is from hairdressers and others whose work brings them frequently into contact with hair dyes. Again, their health and mortality records will be related to extent of exposure.

C. EXPOSURE TO METALS, METALLIC SALTS AND OXIDES AND OTHER INORGANIC CHEMICALS

91. MORTALITY, MEDICAL, AND REPRODUCTIVE STUDY OF LEAD WORKERS

Leffingwell, S., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

MORTALITY STUDY OF LEAD WORKERS: Lead phosphate administered subcutaneously to rats has resulted in the induction of renal tumors. Renal tumors in rats have also been induced by lead acetate-containing diet. Lead oxide appears to act synergistically with benzo(a)pyrene in pulmonary tumorigenesis in Syrian hamsters, since lead is reportedly cumulative in the lung. Workers in lead smelters and battery plants may breathe or ingest lead as a result of poor work hygiene practices. Possible carcinogenic or co-carcinogenic effects deserve examination. Although the authors of a study concerning carcinogenesis among lead battery plant workers concluded that their results do not support a specific cancer risk, the data indicate that such a risk may be present. In order to further assess the possible excess cancer risk related to lead exposure, a further retrospective cohort study is planned on workers exposed to lead and its compounds. A contract for establishing a master file and doing follow-up was given to Westat, Inc. The cohort has been identified and follow-up is under way.

REPRODUCTIVE STUDIES: Since as early as the mid 1800s, the effects of lead exposure on human reproduction have been observed. In 1860, Constantin Paul collected case histories on the reproductive effects in both male lead workers and their wives and in women workers who have had exposure to lead. Recently, Lancranjan et al, (1975), in a study of 150 male lead battery plant workers found that those in groups strongly affected by lead exposure had 'decreased fertility due to anthenospermia (reduced viability of sperm), hypospermia (both reduced numbers), or teratospermia (malformed), frequently associated.' All these reports suggest effects of lead on reproduction through both male and female exposure. Two reproductive history studies are being done, one to examine the effects on the male, and one to examine the effects on the female worker. Most of the data for the study of male workers have been collected, coded, and prepared for analysis. The study population for the study of effects of lead exposure on women workers has not yet been selected. Due to external delays, and due to limited personnel at NIOSH, this study will be postponed one year. (Text Abridged.)

92. MORTALITY STUDY OF LEAD WORKERS

Selevan, S. G., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Lead phosphate administered subcutaneously to rats has resulted in the induction of renal tumors and renal tumors have also been induced in rats by lead acetate-containing diets. Lead oxide appears to act synergistically with benzo(a)pyrene in pulmonary tumorigenesis in Syrian hamsters; lead is reportedly cumulative in the lung. Workers in lead smelters and battery plants breathe or ingest lead as a result of poor hygiene. Possible carcinogenic or co-carcinogenic effect deserves examination. Although the authors of a study on cancer among lead battery plant workers concluded that their results do not support a specific cancer risk, the data suggest that such a risk may be present. In order to further assess the possible excess cancer risk to lead exposure, a further retrospective cohort study is planned on workers exposed to lead and its compounds.

93. MORTALITY RISK STUDY OF COPPER SMELTER WORKERS

Frappier Davignon, L., Armand Frappier Institut, Centre de Recherche en Epidemiologie et Medecine Preventive, *531 Blvd. des Prairies, Case Postale 100, Laval des Rapides, Quebec*, H7N 4Z3, Canada

The study aims to determine if an excess risk of mortality from certain diseases, especially lung, renal or prostate cancer, exists among copper smelter workers. These workers are exposed to lead, arsenic, cadmium and sulphur dioxide. Five levels of exposure to these different contaminants have been determined: (1) no exposure; (2) exposure to concentrations always below the threshold limit values (TLV) accepted by the National Inst. of Occupational Safety and Health (US); (3) average exposure below TLV but with possible incursion over; (4) average exposure always over TLV; (5) exposure known but never measured. Employees who have worked at least one year for the company between 1 January 1952 and 31 December 1957 are followed up to 31 December 1977. In all 2,246 workers will be studied. The risk of mortality related to different cancers will be evaluated by comparing the number of cancers observed in a cohort to the number expected in a population of the same age and sex, for each year, in the Province of Quebec.

94. CANCER IN ARSENIC-EXPOSED POPULATIONS

Enterline, P. E., University of Pittsburgh, Graduate School of Public Health, Dept. of Biostatistics, *4200 5th Ave., Pittsburgh, Pennsylvania*, 15260, United States of America

The mortality experience of workers at a copper smelter in Tacoma, Washington, where nearly all the arsenic trioxide in the United States is produced, is being studied. Men employed a year or more between January 1, 1940, and December 31, 1964, have been followed for deaths through December 31, 1977. The cancer mortality experience of this cohort is being related to duration and intensity of arsenic exposure and latent period. Historic urinary arsenic measurements on workers are used to estimate exposures.

In addition, the mortality experience of persons living near the smelter is being studied to see if any effect of atmospheric contamination on cancer mortality can be detected. This includes: a) a follow-up of children from an elementary school in the area using a cohort identified from school records between 1900 and 1919, and b) a study of mortality by census tract for Tacoma in which mortality in areas adjacent to the smelter will be compared to mortality in non-adjacent areas.

95. ANACONDA SMELTER STUDY

Higgins, I. T., Welch, K. B., Oh, M. S., University of Michigan, Ann Arbor Campus, School of Public Health, Dept. of Epidemiology, Environmental & Industrial Health, *Ann Arbor, Michigan*, 48104, United States of America

In 1969 a study of 8,047 men working at a copper smelter was published by the National Cancer Inst. (NCI). An excess of respiratory cancer related to occupational exposures to arsenic trioxide was demonstrated. There was also some indication that exposures to sulphur dioxide were related to the excess respiratory cancer mortality. The University of Michigan will study a random sample of 1,800 men originally invetigated by NCI. The arsenic exposure, work histories and vital status of these men will be updated to 1977. In addition, information on smoking habits will be obtained retrospectively. Standardized mortality ratios will be calculated based on exposures to arsenic, sulphur dioxide, and cigarette smoking.

96. INDUSTRIAL HYGIENE STUDY OF BE-CU EXPOSURES - NCI

Donaldson, H., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Though beryllium in most of its forms exhibits delayed toxicity, either as the metal or as a chemical compound such as the oxide, beryllium-copper alloy appears to exhibit these properties only when the alloy is heated above its melting point so as to produce fume. In this study, it is planned to examine the records of 50 cases of berylliosis allegedly resulting from exposure to Be-Cu alloy that are in the Beryllium Case Registry, and also to examine airborne beryllium exposure data collected between 1960 to 1972 in the state of Pennsylvania in plants fabricating Be-Cu in various ways. No beryllium disease has been reported from the Pennsylvania plants.

It is planned to have records of the 50 berylliosis cases in the BCR examined by the Medical and Biometry sections of DSHEFS in an attempt to determine any excess of cancer in this population, and also to obtain a medical opinion as to whether the cases should continue to be classified as berylliosis cases.

The Pennsylvania monitoring data will be used as a guide in determining controls needed in various types of Be-Cu fabrication operations. For example, it may be adequate to monitor Be-Cu operations by collecting respirable air samples instead of total air samples and still protect the worker from occupational disease. Conclusions from this research will be the recommendation of work practices and monitoring methods which may be less restrictive than those presently used.

97. CANCER RISK IN NON-FERROUS METALLURGY AND CHROMIUM INDUSTRIES

Gabor, S. I., Nagy, L., Popovici, A., Ghelberg, N., Coldea, V., Kovats, A., Valentini, E., Ciontea, G., Modorcea, V., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Health, *Pasteur 6, 3400 Cluj Napoca, Romania*

Exposure of workers to lead, cadmium, copper, arsenic, chromium and sulphur dioxide from non-ferrous metallurgy and chromate industries, as well as that of the population living in the surrounding polluted areas, represents a risk of high cancer incidence. This investigation aims at assessing the mortality patterns of retired workers employed in non-ferrous metallurgy (lead and copper smelting) and chromium compound production plants compared to the mortality rate of the general population. Environmental measurements will be carried out in parallel with biotoxicological tests of exposure and sputum cytology screening examinations. As estimated, 1,500 workers will be surveyed.

98. A MORTALITY STUDY OF NICKEL WORKERS IN ONTARIO

Roberts, R. S., Mastromatteo, E., McMaster University, Dept. of Clinical Epidemiology & Biostatistics, *1200 Main St. W., Hamilton, Ontario*, L8S 4L8, Canada

This study ultilizes a fairly conventional historical prospective design to compare mortality patterns in nickel workers over a 27 year follow-up period. The study cohort consists of approximately 70,000 men working at Sudbury and Port Colborne. Eligible subjects are males with six months or more of accumulated service who worked for the company (or who were receiving a pension) on or after 1 January 1950. The mortality experience of these men through to the end of 1976 will be ascertained from the Statistics Canada registry of death certificates using a record linkage procedure based on full name, date of birth and 'last known alive' date. A series of tactics are being undertaken to estimate the accuracy of the matching. The analysis of this data will relate features of the detailed occupational histories of these men to cause-specific mortality. Of particular interest are the relationships of cumulative nickel sulphide and nickel oxide to respiratory cancer, but other cancers and contaminants will also be considered. In addition, exposure in terms

of years of duration in particular occupations (i.e., the sinter plant) will be analyzed.

99. MORTALITY STUDY OF HIGH NICKEL ALLOY WORKERS

Redmond, C. K., Weiand, H. S., Sass, R. E., University of Pittsburgh, Graduate School of Public Health, Dept. of Biostatistics, *4200 5th Ave., Pittsburgh, Pennsylvania*, 15260, United States of America

There is evidence of increased incidence of respiratory cancers, including cancers of the nasal sinuses, among workers in the nickel refining industry. In order to determine whether any such relationship might exist among workers in the high nickel alloy (more than 20% Ni) industry, cause-specific mortality and especially site-specific cancer mortality among workers in eleven study plants across the USA will be investigated. The mortality experience of nickel-exposed workers in the study plants will be compared to the population of workers involved in all phases of operation in the study plants, and to the total United States mortality experience. The study is a historical prospective follow-up on a cohort of approximately 20,000 workers with at least one year of job experience during the period 1956-1960. The work will involve developing a coding system for classifying jobs to permit comparisons across plants with similar occupational groups and follow-up procedures for former workers to determine vital status for all individuals in the cohort.

100. MORTALITY STUDY OF NICKEL COMPOUND MANUFACTURING

Buncher, C. R., Laskarzewski, P., University of Cincinnati, College of Medicine, Dept. of Epidemiology & Biostatistics, *Eden & Bethesda Aves., Cincinnati, Ohio*, 45221, United States of America

Using about 2,000 employee work history records, employees involved in the manufacture of nickel salts and nickel catalysts will be compared to other workers in the same company with respect to causes of death. A number of studies in the nickel smelting industry and with nickel carbonyl have shown increases in nasal and respiratory carcinoma. Studies of other persons involved in various uses of nickel have been few. Death certificates are being obtained for all former employees of this U.S. company who have worked at least one year and these will be subjected to a life table and proportionate mortality analysis.

101. MORTALITY PATTERN OF NICKEL PLATING WORKERS

Burges, D. C., Employment Medical Advisory Service, *Broad Rd., Birmingham B15 1DL, England, United Kingdom*

A population of some 900 workers at a nickel plating factory is being studied with the assistance of the Office of Population Censuses and Surveys which will provide death certificates, to test whether there is any carcinogenic risk, particularly lung cancer, involved in decorative electrolytic nickel plating, in view of the fact that nickel has been reported as a carcinogen in other nickel industries, principally the refining of nickel. This is a 'historic-prospective' study.

102. MORTALITY AND MORBIDITY SURVEY INTO THE OCCUPATIONAL RISK OF NICKEL FROM CHEMICAL PRODUCTION IN LUDWIGSHAFEN, GERMANY (ABBREV)

Thiess, A. M., Frentzel Beyme, R. R., Link, R., Badische Analin & Soda Fabrik Ag, Werksaerztliche Abteilung, *Bruckstrasse 56, 6700 Ludwigshafen, Federal Republic of Germany*

The study is to assess cancer incidence in occupational risk groups as suggested by carcinogenic effects of nickel from animal experiments. The chemical workers ever exposed to the substance are followed up for mortality experience (cause of death) and for morbidity (as far as data are available). The follow-up includes careful tracing of persons who either retired or resigned.

103. CANCER OF THE LARYNX AND OCCUPATION

Olsen, J., Sabroe, S., Lajer, M., Fasting, U., Odense Universitet, Inst. of Hygiene & Social Medicine, Dept. of Social Medicine, *Winslowsvej 17, 5000 Odense, Denmark*

The purpose is to study the etiology of larynx cancer in relation to occupation. In a case-control study involving all new larynx cancer patients in Denmark below the age of 70 occupational exposure histories are compared with those of controls matched for age, residence and broad occupational group, taken mainly from union files. The focus is exposure to chrome and nickel. Information is obtained by interview which includes detailed questions about smoking and alcohol comsumption. The study will involve 200 patients and 800 controls.

104. LUNG CANCER IN THE ANTIMONY INDUSTRY

Cunningham, J. P., Billington, N. A., Fletcher, F. J., Anzon Ltd., *Cookson Hse., Willington Quay, Tyne and Wear, Wallsend NE28 6UQ, England, United Kingdom*

A prospective epidemiological survey of workers engaged in the production of antimony metal, antimony oxide, and antimony sulphide is being undertaken to ascertain whether there is an excess of lung cancer by comparison with local death rates and death rates in other occupations. The survey includes all persons working at the plant on 1/1/1961 or joining after that date, and is likely to continue until 1985 or later. Persons leaving employment are traced. The calculations of expected deaths are age-specific and related to man-years of exposure. The survey covers an adjacent zircon plant, as a control. Other factors studied are smoking, sulphur, arsenic and area of residence.

105. EPIDEMIOLOGY OF LUNG CANCER IN ANTIMONY PROCESS WORKERS

McCallum, R. I., Petrie, A., University of Newcastle upon Tyne, Dept. of Occupational Health & Hygiene, *6 Kensington Terr., Newcastle upon Tyne NE1 7RU, England, United Kingdom*

This is a mortality study of men exposed to inorganic antimony compounds during the processing of the imported ore to determine whether or not there is an excess of deaths from lung cancer, and the influence on this of smoking habits and other factors in the environment, including exposure to arsenic.

106. ANTIMONY STUDY

Duncan, K. P., Health & Safety Center, *97 Horseferry Rd., London SW1P 2DY, England, United Kingdom*

OBJECTIVE: To discover whether workers in an antimony smelting factory have excess mortality from lung cancer.

107. INVESTIGATION OF MORTALITY AND MORBIDITY PATTERNS IN CADMIUM WORKERS IN THE UNITED KINGDOM

Kazantzis, G., Adams, R. G., Holden, H., Hughes, E. G., King, E., Malcolm, D., Wright, D., University of London, London School of Hygiene & Tropical Medicine, T.U.C. Centenary Inst. of Occupational Health, *Keppel St., London WC1E 7HT, England, United Kingdom*

Cadmium is a metal shown to be carcinogenic in animal experimental studies. Limited observations in man suggest that there may be an increased mortality from cancer of the prostate and of the lung in cadmium workers. The study will, in the first instance, seek to ascertain causes of death in cadmium workers, with particular reference to malignant disease and renal pathology. All persons who have worked with regular exposure to cadmium for a minimum period of one year in selected industries will be included in the study. A retrospective register of cadmium workers from records held by the respective companies will be compiled, and mortality data on this defined population obtained and compared with that of an appropriately matched control group.

108. MORTALITY EXPERIENCE AMONG A COHORT OF CADMIUM SMELTER WORKERS

Lemen, R. A., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Animal and human studies have shown increased risks of malignant and non-malignant disease from exposure to cadmium. Specifically NIOSH cohort mortality studies have shown increased risks of prostatic and respiratory cancer among a cohort of cadmium smelter workers having been exposed for two years or more in the smelter. Employment records to identify all workers in the facility are coded and follow-up has been initiated to determine vital status of the remaining approximately 1,300 individuals who have ever worked in the smelter. Patho-

logical and medical histories still remain to be collected concerning those deaths which have been identified so far.

109. HUMAN CADMIUM EXPOSURE AND CANCER

Kjellstrom, T., University of Auckland, *P.O. Box 2175, Auckland, New Zealand*

OBJECTIVE: To evaluate the occurrence of chronic illness (particularly cancer) in population groups with exposure to high levels of cadmium compounds.

110. EXPOSURE TO IRON OXIDE AND CANCER INCIDENCE

Axelson, O., Sjoeberg, A., University of Linkoping, University Hospital, Dept. of Occupational Medicine, *58185 Linkoping, Sweden*

Several epidemiological and experimental reports suggest that iron oxide is carcinogenic. However, the reported increase in lung cancer mortality among the various populations (miners, foundry workers) with exposure to iron oxide might be due to concomitant exposures, e.g., randon daughters in the mines, polycyclic hydrocarbons in the foundries, etc. High levels of exposure to iron oxides have occurred in a Swedish plant producing sulphuric acid from pyrites. This situation provides another opportunity to evaluate the possible cancer hazard of iron oxides. This is a case-control study, using two controls for each case matched by sex, age and place of residence. It is undertaken within a general evaluation of the relationship between cancer and various occupational exposures in the city of Helsingborg.

111. STUDY OF WORKERS IN A SODERBERG ALUMINUM SMELTER

Buncher, C. R., University of Cincinnati, College of Medicine, Dept. of Epidemiology & Biostatistics, *Eden & Bethesda Aves., Cincinnati, Ohio*, 45221, United States of America

Several recent studies have suggested that workers in aluminum smelting are subject to an excess risk of lung cancer and some types of leukemia and lymphoma. The indications are that pot room workers are most subject to the risk. This study of 2,700 workers is a follow-up of previous reports with the purpose of trying to relate specific work assignments in this plant with possible excess cancer risk in an occupational mortality study. Death certificates are being obtained and will be compared by work classification within each department of the production facility. This study is part of a tri-partite research project involving industry, labor unions, and government.

112. LUNG CANCER IN A COHORT OF WELDERS

Beaumont, J. J., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Welders constitute approximately one per cent of the United States male workforce, and on a daily basis they are exposed to a variety of metal oxides, gases, and other substances evolved from the welding process. To assess their lung cancer mortality, a cohort of 3,247 welders with at least three years experience was established from the records of a metal trades union representing workers in shipyards, metal fabrication ships, and field construction. Comparison has been made with death statistics and preliminary results indicate an excess lung cancer rate of 31 per cent, which increases to 69 per cent when only those person-years after 20 years latency are considered.

113. MORTALITY AMONG WORKERS IN THE METAL POLISHING, BUFFING, AND PLATING INDUSTRY

Blair, A. E., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst., *9000 Rockville Pike, Bethesda, Maryland*, 20205, United States of America

Workers in the metal polishing, buffing, and plating industry are exposed to a number of potentially hazardous substances (metal dusts, cyanide solutions, solvents and degreasers). To evaluate the mortality experience of this group and to provide clues concerning the carcinogenicity of certain occupational exposures, the distribution of causes of death among 3,000 past members of the Metal Polishers, Buffers, Platers, and Helpers International Union will be compared with the distribution in the general population.

114. THE PROPORTION OF METAL WORKERS AMONG PATIENTS WITH TESTICULAR CANCER AND AGE-MATCHED CONTROLS

Rhomberg, W. U., Schmoll, H. J., Medizinische Hochschule Hannover, Dept. of Radiology, *Karl-Wiechert-Allee 9, D3000 Hannover 61, Federal Republic of Germany*

Preliminary analyses suggest that the occupational histories of patients with testicular cancer show an unusually high proportion of metal workers. The data have been collected from 64 patients treated in the Medizinische Hochschule between 1967 and 1974. The objectives of the present study are to increase the number of interviews investigating the occupational background of patients with testicular cancer, and to establish a control group consisting of patients with diseases other than cancer, of comparable age and treated in the same hospital as the patients with testicular cancer.

115. CANCER MORTALITY IN UNITED STATES CARBON BLACK WORKERS

Robertson, J. M., Ingalls, T. H., University of Western Ontario, Faculty of Medicine, Dept. of Preventive Medicine & Epidemiology, *1151 Richmond St., London, Ontario*, N6A 3K7, Canada

The cancer mortality experience of employees of four companies engaged in the production and distribution of carbon black in the United States was examined in this retrospective cohort study. All male employees with 12 or more months of service between 1935 and 1974 were study participants. The study group consisted of employees exposed to carbon black, i.e., employed on-site at a carbon black plant; the comparison group was composed of men employed in company operations other than carbon black production. The companies supplied mortality data on active and retired employees from their life insurance files. They also supplied annual employee censuses by age and years of service from which man-years at risk were calculated in 5-year age groups for quinquennial periods from the beginning of the study to employee withdrawal or termination of the study. Assuming an underlying poison distribution, the cancer mortality of the exposed (carbon black) group and the unexposed (comparison) group was compared with the expected mortality based on the sex-, age-specific cancer mortality rates of the male populations of the States in which the carbon black plants were located. Mortality due to all malignant neoplasms (I.C.D. 140-209) was lower than expectation in exposed workers but not significantly so. In unexposed workers, observed deaths due to all malignant neoplasms were significantly lower than expected (P less than 0.05). Deaths due to malignant neoplasms of the digestive organs (I.C.D. 150-159) and of the respiratory system (I.C.D. 160-163) did not exceed expectation in either group. No trend of increased mortality with increasing years of service (exposure) was evident in exposed workers (chi-square equals 0.66, d.f. equals 1; 0.25 less than p less than 0.50). The results of this study do not support an increased risk of death due to malignant neoplasms in carbon black workers. Analysis continues.

116. CARBON BLACK STUDY

Duncan, K. P., Health & Safety Center, *97 Horseferry Rd., London SW1P 2DY, England, United Kingdom*

OBJECTIVE: To see whether excess lung cancer mortality in the rubber industry and printing industry is associated with carbon black.

117. COHORT STUDY OF LUNG CANCER AMONG MEN OCCUPATIONALLY EXPOSED TO HYDRAZINE

Wald, N., Doll, R., University of Oxford, Radcliffe Infirmary, Cancer Epidemiology & Clinical Trials Unit, *Oxford OX2 6HE, England, United Kingdom*

Following evidence in animals that exposure to hydrazine increased the incidence of lung and liver tumors, a cohort study involving 423 men who have been occupationally exposed to hydrazine is being carried out. Identification information relating to these men has been collected and their records tagged at the National Health Service Central Register so that notification of cancer and death can be obtained.

II. CANCER INCIDENCE RELATED TO SPECIFIC OCCUPATIONS

A. RUBBER WORKERS

118. OCCUPATIONAL LUNG CANCER IN THE RUBBER INDUSTRY

Andjelkovich, D. A., Delzell, E. S., Tyroler, H. A., University of North Carolina, Chapel Hill Campus, School of Public Health, Dept. of Epidemiology, *Rosenau Hall, 201H, Chapel Hill, North Carolina*, 27514, United States of America

This study was prompted by conflicting findings in relation to occupational lung cancer in the industry. While an overall excess of lung cancer was found in Great Britain, an overall deficit was observed by us in the U.S. Accordingly, it was decided to investigate the relationship between mortality from this disease and specific occupational exposures. The main objective of this study is to identify, retrospectively, specific groups of workers who may experience an excess risk of mortality from lung cancer. In addition, the British report of an association between this disease and employment in areas where curing of green rubber products is performed is being evaluated and other published findings on a relationship between lung cancer and work in jobs involving compounding and mixing of raw rubber stocks is being examined. A case-control study design with over 100 cases and 400 controls is being used, matched on pertinent variables to eliminate confounding factors unique to occupational studies. The analysis involves examination of detailed employment records to determine whether cases were more likely to have worked in specific areas within the plant under study, which may now contain (or which may have contained in the past) respiratory system carcinogens. The design also includes an examination of certain non-occupational factors which may be responsible for the observed excess.

119. BRITISH RUBBER MANUFACTURERS' ASSOCIATION HEALTH RESEARCH PROJECT

Parkes, H. G., Waterhouse, J. A., British Rubber Manufactures Assn. Ltd., Occupational Health Research Unit, *Scala House, Holloway Circus, Birmingham B1 1EQ, England, United Kingdom*

The aim of this study is to examine the health records of workers in the British rubber industry and to compare their mortality experience with that of the general population. All major type companies are included, together with some associated products. The study also compares the experience of three distinct cohorts of entry to the industry - first for those who entered the study between 1946 and 1950, the second between 1951 and 1955, and the third between 1956 and 1960. Although the main aim of the study is to investigate possible excesses of cancer hazards, all causes of death are recorded and certain other groups of causes are being examined. It is hoped to be able to associate any high risk areas with the results of environmental monitoring tests that have been made in the last year or so and with such details as can be obtained of past conditions in each factory. Analysis of the results to date has shown a small, but significant, excess of malignant disease of the stomach and of the lung, particularly in recent entry cohorts. Except for the first entry cohort there is no raised incidence of bladder cancer. This is in line with the banning of the use of 2-naphthylamine in 1949. Detailed studies of the conditions of work in those areas which show an excess of malignant disease in each factory are now being made and a further follow-up of mortality records is being undertaken.

120. STOMACH CANCER AMONG RUBBER WORKERS - A CASE-CONTROL STUDY

Blum, S. B., Tyroler, H. A., Shy, C. M., University of North Carolina, Chapel Hill Campus, School of Public Health, Dept. of Epidemiology, *Rosenau Hall, 201H, Chapel Hill, North Carolina*, 27514, United States of America

Whereas the incidence of stomach cancer has been steadily declining in the U.S. during the past few decades, our analyses have indicated that rubber workers remain at a considerably higher risk than the general population. Because of the diverse chemicals to which these workers are being exposed, many of which are known or suspected carcinogens, an analytical study is being conducted to determine whether this excess risk may be caused by industrial exposures to polycyclic hydrocarbons, nitrosamines, asbestos, or carbon black. All of these substances have been, or are being, used or generated by the industrial processes in the rubber industry.

121. FATAL LYMPHOMAS IN RUBBER WORKERS, A CASE-CONTROL STUDY

Tyroler, H. A., Keil, U., Andjelkovich, D. A., University of North Carolina, Chapel Hill Campus, School of Public Health, Dept. of Epidemiology, *Rosenau Hall, 201H, Chapel Hill, North Carolina*, 27514, United States of America

Recent descriptive mortality analyses in five major US rubber companies have demonstrated a consistent excess of deaths among rubber workers from malignant neoplasms of the lymphatic and hematopoietic system (LHS). A case-control study has demonstrated an association between lymphatic leukemia and a history of having worked in jobs entailing solvent exposure. 87 persons, dying in period 1964-1973 with an LHS neoplasm diagnosed as lymphoma, have been individually matched with two pairs of controls, selected from non-cases within the source population from which the case derives. Complete work history information will be utilized for all study subjects. Analysis of case-control differences in work history will examine the association of leukemia types with solvent exposure and similarities and differences between exposure histories of fatal cases of lymphoma and leukemia.

122. CANCER AMONG RUBBER WORKERS AND ESTIMATION OF CANCER RISK BY URINARY THIOETHER EXCRETION OF WORKERS

Kilpkari, I. V., Hakama, M., Tampere Yliopisto, Dept. of Public Health, *Vuolteenkatu 11, 33100 Tampere 10, Finland*

OBJECTIVES: 1. To determine the risk of cancer and risk at mortality among workers at a Finnish rubber factory. 2. Urinary thioether excretion is correlated with exposure under working conditions. 3. Whether urinary thioether excretion is correlated with incidence to cancer among rubber workers.

APPROACH: Epidemiological methods are used to evaluate cancer incidence and mortality by cause of death in groups of workers with different exposure. Urinary thioether excertion is correlated with work conditions and with risk of cancer for purpose of prevention.

123. RETROSPECTIVE EPIDEMIOLOGICAL STUDY OF HEALTH HAZARDS IN THE RUBBER INDUSTRY

Holmberg, B. E., Nilsson, L. R., Gumaelius, K. Q., Elofsson, S., Westerholm, P., Englund, A., National Board of Occupational Safety & Health, Unit of Occupational Toxicology, *17184 Solna, Sweden*

All workers in two large rubber companies employed between January 1, 1930, and December 31, 1972, who worked for more than one year, will constitute the cohort. The cohort will be subdivided according to department: mixing department and other production departments. White collar workers form a control group. These lists of workers will be completed by the personal identification number and compared with the official death registry and the cancer registry.

124. RUBBER AND CABLE MAKING STUDY

Duncan, K. P., Employment Medical Advisory Service, *Chepstow Pl., London W2, England, United Kingdom*

OBJECTIVES: To monitor the incidence of bladder cancer in subjects who enter the industry after known carcinogens have been removed and also to monitor the general cancer incidence.

B. URANIUM AND OTHER MINE WORKERS

125. ONTARIO MINERS STUDY

Muller, J., Wheeler, W., Buchanan, R., Gentleman, J. F., Smith, M., Kusiak, R., Ontario Occupational Health & Safety Div., Special Studies & Services Branch, *4000 University Ave., Toronto, Ontario*, M7A 1T7, Canada

It is known that uranium miners have an increased lung cancer risk. This study will attempt to calculate the relationship between the time course of exposure to short-lived radon daughters and the time course of excess lung cancer risk. Several control populations will be used: Ontario males, Northern Ontario males and Ontario miners who have not worked in an uranium mine. The study will also investigate cancer risks

among non-uranium miners. The employment history data and coded x-ray results (silicosis ratings) from the annual medical examinations required of all active miners in Ontario are being recorded in computer files for all uranium miners and for all miners who have reported for a medical examination in 1955 or later and had 5 or more years of mining experience. In the data files, there are about 16,000 men who qualify as uranium miners and about 34,000 men who meet the latter qualifications. The employment histories and measurements of air concentrations of short-lived radon daughters will be used to make an estimate of each uranium miner's annual exposure between 1955 and 1967. From 1968 onwards exposure was estimated by the mining company. When all these data have been assembled, there will be, for each uranium miner, a record of exposure to short-lived radon daughters for each year that he was employed as an uranium miner. Information concerning deaths in the study population will be obtained by matching the personal identifying information of each miner with information contained in the Canadian Death Registry maintained by Statistics Canada. The data files will be completely assembled in the early part of 1980 and a review will be started then. The study is on-going and the data are to be reviewed regularly.

126. URANIUM EPIDEMIOLOGY STUDY

Buechley, R. W., Key, C. R., Samet, J. M., Morgan, M. V., University of New Mexico, School of Medicine, Epidemiology Section, *University Hill N.E., Albuquerque, New Mexico*, 87131, United States of America

4,071 uranium miners with at least one year's underground experience since 1957 in the Grants, New Mexico uranium belt will be studied to examine health effects of low level radiation exposures for which only extrapolations are now available. Since mining in this district began, precision of radiation measurement and stringency of radiation standards have increased. Of the 4,071 miners in the study, 1,800 started work before 1961, at mean radiation levels near 40 working level months (WLM) per year. Another 1,300 started in 1961-1970, at mean radiation levels declining over the years from 40 to 4 WLM per year. The remainder started in 1971 or later, at mean radiation levels of 2.5 WLM per year and not exceeding the allowable 4 WLM per year. Standard physical examinations, with cigarette smoking and previous mining histories, are available from the beginning. Of the 139 miner deaths reported to date, 84 were from accidents, poisonings or violence. Of the 55 other deaths, 22 were due to lung cancer, all in miners employed before 1961 in Grants or elsewhere and concentrated in miners with over 200 cumulative WLM. 20 of the 22 lung cancer deaths were in cigarette smokers. Proposed work for 1980-1981 includes determining current status of miners through the US Social Security Administration, etc., refining their amounts of radiation exposure, and planning a very long-term cohort study.

127. EPIDEMIOLOGICAL STUDIES OF URANIUM MINERS AND MILL WORKERS

Archer, V. E., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Health Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Uranium miners have been found to have an excess of lung cancer and mill workers to have an excess of lymphomas. A much larger group of mill workers is now being studied by a retrospective cohort study to determine the magnitude of the lymphoma excess. Identification of the substance responsible is being attempted. Two groups of uranium miners are being studied, one of about 4,300, and a much larger one of about 15,000. These groups are being used to determine exposure-response curves, and the different factors which influence the shape of those curves; effects of exposure on the sex-ratio of offspring, the effect of age at first exposure on incidence and latent period, and the dose rate effect.

128. FOLLOW-UP STUDY OF CANCER IN URANIUM MINERS AND RELATED WORKERS

McMichael, A. J., Clark, P. D., South Australian Health Commission, *52 Pirie St., Adelaide, South Australia 5000, Australia*

Approximately 2,600 men operated the Radium Hill uranium mine in South Australia, during 1953-1962. The detailed employment histories of these men, plus the systematic radiation monitoring data form the basis of an on-going follow-up study. Searches of cancer and death registrations throughout Australia, plus searches of voter registrations, driver's licence rolls, and overseas arrivals and departures, give an 80% trace rate. Preliminary proportional mortality analysis of a workforce sample suggests an increase in respiratory cancer.

129. EPIDEMIOLOGIC METHODS - U.S. URANIUM MINERS

Whittemore, A. S., Stanford University, School of Medicine, Dept. of Family Community & Preventive Medicine, *300 Pasteur Dr., Stanford, California*, 94305, United States of America

The proposed study would use probabilistic models of cellular carcinogenesis, combined with maximum likelihood statistical procedures for estimation of model parameters, to analyze lung cancer mortality among U.S. uranium miners. The parameters used in the models aad estimated from the data would have biological interpretations. They would be used to examine the following issues: 1) the dose-response relationship for exposure to radon daughters, particularly as it applies to low level exposures; 2) the nature and extent of interaction between radiation and smoking exposures in respiratory carcinogenesis; 3) the presence or absence of dose rate effect; 4) the effect of age at start of irradiation upon subsequent lung cancer risk; 5) the evolution of risk after termination of exposure.

Particular attention will be paid to implications for risk due to occupational radiation exposures at the current standards.

130. LONG-TERM STUDY OF MINERS EXPOSED TO RADON-222

Radford, E. P., St. Clair Renard, K. G., University of Pittsburgh, Graduate School of Public Health, Dept. of Epidemiology, *4200 5th Ave., Pittsburgh, Pennsylvania*, 15260, United States of America

Eight 5-year cohorts of underground miners born 1880-1919, who are still living or have died in Malmberget, Sweden, have been followed up to 1976. Exposure doses are calculated from radon-daughter measurements in air and water and from radioactivity in water springs in the mines measured in 1914. Attention has been paid to the different depths of the mine over the years and ventilation in different places of work. A substantial number of lung cancer cases have occurred in miners who never smoked or were ex-smokers. A survey of smoking prevalence in active and retired miners has been done to permit assessment of the role of smoking in relation to radon-daughter exposures in the genesis of bronchial cancer. Follow-up of all 1,441 miners is now complete and the data are being analysed.

131. SPATIAL AND TEMPORAL VARIATIONS IN FOUR COMMON CANCERS IN BLACK GOLD MINERS FROM SOUTHERN AFRICA

Harington, J. S., McGlashan, N. D., Bradshaw, E. J., South African Inst. for Medical Research, *Hospital St., P.O. Box 1038, Johannesburg 2000, Transvaal, South Africa*

In previous work on the gold miners, the pattern of cancer in Black gold miners over the eight-year period 1964-71, constituting 2,926,461 man-years of employment, was studied. Of the 1,344 cancers found, primary liver cancer accounted for 52.8%, oesophageal cancer 12.1%, cancer of the respiratory system 5.4%, and cancer of the bladder 4.8%. Analysis of the spatial distribution of these four cancers, both on subcontinental and local scale, showed distinct gradients of significantly higher and lower incidence than expected. In the case of primary liver cancer in Mozambique and oesophageal cancer in Transkei, the spatial distribution reflects closely that found in the general resident population of each territory. The crude incidence rate of primary liver cancer in gold miners from Mozambique dropped sharply over the period of the survey. The survey continues.

132. RISK OF PRIMARY LUNG CANCER AMONG IRON MINERS

Cavelier, C., Pham, Q. T., Mur, J. M., Meyer Bisch, C., Inst. Nacional de Recherche et de Securite, Service de Pathologie Professionelle, *Ave. de Bourgogne, Vandoeuvre-les-Nancy, 54500 Nancy, France*

The purpose of this study is to determine whether working in iron mines involves an increased risk of primary lung cancer. A retrospective mortality survey will be carried out in Lorraine

on 2,000 miners for whom data from periodic medical examinations are available for a period of 20 years. The adjusted absolute and relative incidence rates for primary lung cancer among miners and surface workers will be compared.

133. LONG-TERM MORTALITY STUDY OF MINNESOTA IRON ORE MINERS

Schuman, L. M., University of Minnesota, Minneapolis Campus, School of Public Health, Dept. of Epidemiology, *1325 Mayo Memorial, Minneapolis, Minnesota*, 55455, United States of America

This is intended to be a collaborative study between the University of Minnesota and the Environmental Epidemiology Branch of the National Cancer Institute. The contract calls for basic data collection activities, whereby information from company employment records is abstracted and put into computer readable form. The work would include data editing and updating files with vital status information.

134. RADIATION EXPOSURE AND MORTALITY IN FLUORSPAR MINERS

Wigle, D. T., Stocker, H., McCullough, R., Hollywood, B., Canadian Dept. of National Health & Welfare, Lab. Centre for Disease Control, *Tunneys Pasture, Ottawa, Ontario*, K1A 0L2, Canada

The objective of the study is to evaluate the risk of death due to lung cancer as a function of cumulative exposure to radon and radon daughters in the fluorspar mines of St. Lawrence, Newfoundland. The mortality and adaptation exposure experience of over 2,000 men employed between 1933 and 1977 will be reviewed. Fluorspar mining in St. Lawrence (population 2,078, 1956 census) began in 1933 and by the period 1952-60, lung cancer accounted for 21 of the 71 total deaths: only 0.73 lung cancer deaths were expected based on proportional mortality rates for the province (O/E equals 29). Investigation in 1959 revealed the presence in air of radon and radon daughters at levels up to 193 SWL (1 SWL equals 100 pc/l for radon and 1.3 x 10 to the 5th power MeV total potential alpha-energy per liter for daughters) in non-working, unventilated areas. The average exposure of miners was estimated to be 2.5-10 SWL. Improved ventilation and monitoring of individual exposure were started in 1960. Current studies are directed towards evaluation of control procedures and analysis of the associations between radiation exposure and mortality utilizing individual exposure data and man-years at risk.

135. MORBIDITY AND MORTALITY AMONG PHOSPHATE MINERS

Matanoski, G. M., Seltser, R. S., Mitchell, T. M., Billings, C., Block, G. M., Johns Hopkins University, School of Hygiene & Public Health, Dept. of Epidemiology, *615 N. Wolfe St., Baltimore, Maryland*, 21205, United States of America

The purpose of this study is to determine whether there is an excess all-cause and cancer morbidity and mortality among employees of a central Florida phosphate mining company. If such an excess is found, a further objective is to attempt to determine a job site or job title which may be associated with the excess. A primary hypothesis is that such an excess may exist due to worker radiation exposure from uranium and daughter products found in phosphate rock.

The approach is nonconcurrent prospective, in which all employees since 1950 are identified, and their outcomes determined. Mortality is ascertained by means of Social Security Administration records and death certificates. Morbidity is ascertained by means of questionnaries and medical record searches. Additional information will be sought from the employees regarding such factors as smoking history, diet, and exposures to other potentially carcinogenic agents or jobs.

An additional aspect of the study involves whole-body radiation counting on a small number of current long-term employees, to determine whether there is evidence of a body burden of radioactive materials.

136. INCIDENCE OF BRONCHIAL CARCINOMAS IN MINERS IN THE SAARLAND

Dhom, G., Universitaet des Saarlandes, Universitaetskliniken, Pathologisches Institut, *6650 Homburg Saarlands, Federal Republic of Germany*

It is known from English and American investigations that coal miners have a lower mortality from bronchial carcinoma than the rest of the male population. The aim of this study is to see whether similar findings can be obtained for the miners from the Saarland. For this purpose, data available in the Cancer Registry of the Saarland and the health insurance company (Knappschaftskrankenkasse) will be used.

137. INDUSTRIAL POLLUTION AND CANCER

Choi, N. W., Nelson, N. A., Manitoba Cancer Treatment & Research Foundation, Dept. of Epidemiology & Biostatistics, *700 Bannatyne Ave., Winnipeg, Manitoba*, R3E OV9, Canada

Objectives of the study are: (1) to investigate if risks of certain cancers were increased among the employees of a mining and smelting company according to length and place of job in the company and (2) to investigate if risks of certain cancers were also increased for the neighboring community. If so, the increased risk in relation to employment status and/or the relationship of the cases to employees will be further determined. In achieving both objectives, certain important variables such as smoking and dietary habits will be accounted for. Most of the feasibility work has been completed in terms of identification of the cohort group (approximately 30,000), population at risk, linkage of study subjects to a number of different sources of health and vital statistics including our cancer registry and follow-up of the cohort group, etc. As the feasibility of such a study has become apparent, a definitive study will now be conducted.

138. MORTALITY IN CANADIAN MINING COMMUNITIES

Wigle, D. T., Mao, Y., Canadian Dept. of National Health & Welfare, Lab. Centre for Disease Control, *Tunneys Pasture, Ottawa, Ontario*, K1A 0L2, Canada

The objective is to determine the extent of excess mortality, particularly male lung cancer mortality, in Canadian mining communities. A pilot study which revealed substantial excess lung cancer mortality among males in three mining communities will be extended to include about 85 mining and 85 non-mining communities. Direct and indirect age-adjusted mortality rates by sex and cause will be calculated for the mining communities using the non-mining communities and Canada as reference groups. A case-control analysis of occupation will be performed for male deaths due to lung cancer (cases) and other causes (controls) in the mining communities.

139. MINING, SMOKING AND LUNG CANCER

Axelson, O., Sundell, L., Edling, C., University of Linkoping, University Hospital, Dept. of Occupational Medicine, *58185 Linkoping, Sweden*

An earlier report (Axelson and Sundell, Scand. J. Work Environ. Health 4, 46-52, 1978) has indicated a greatly increased lung cancer incidence among zinc-lead miners, as has also been found for iron ore miners in Sweden. It seems resonable to suppose that the occurrence of radon and radon daughters in the mines is primarily responsible for the increased lung cancer mortality among miners. Surprisingly it was found that non-smokers were affected as much or even more than smokers, although smokers, on an average, died of lung cancer before the age of 60, whereas non-smokers died over the age of 70. The explanation might be that smokers in underground work tend to get bronchitis, i.e. an increased thickness of the mucosa, which might protect against alpha radiation. Other mining groups are now being studied using a similar technique to confirm or refute earlier findings.

C. CHROMATE WORKERS

140. A RETROSPECTIVE COHORT STUDY ON MALIGNANT NEOPLASMS IN WORKERS OF A CHROMATE MANUFACTURING PLANT IN TOKYO

Okubo, T., Tsuchiya, K., Jichi Medical School, Dept. of Environmental Health, *3311-1 Yakushiji, Minawi-kawachi-machi, Tochigi-ken 32904, Japan*

The plant chosen for study is the larger of the two chromate manufacturing plants in Japan. In recent years, 24 lung cancer cases have been reported among the chromate workers of the plant. Since the plant was in continuous operation during the period 1915-1975, the follow-up period of over 50 years is

longer than that of previous reports. Various types of personnel records as well as payrolls were used to create the cohort; follow-up is carried out by the Japanese family registration system 'koseki'. Measurements of the working environment have been conducted in the plant since 1958, and it is expected that this study will show clearly any dose-response relationship.

141. LUNG CANCER IN CHROMATE WORKERS

Alderson, M. R., Inst. of Cancer Research, Division of Epidemiology, *Clifton Ave., Sutton SM2 5PX, England, United Kingdom*

This study will examine the relative risk of lung cancer in process workers in the bichromate industry, taking account of factory of employment, calendar period, and duration of employment. A group of workers initially studied in the 1950's will be followed, together with those workers who have since entered three factories in the United Kingdom. All workers leaving this industry will be traced to provide a 30 year follow-up for some workers. Limited data will be available on the specific tasks carried out by individual workers.

142. CHROMIUM CONTENT IN THE LUNG OF CHROMATE WORKERS

Ohsaki, Y., Abe, S., Kimura, K., Tsuneta, Y., Mikami, H., Hokkaido University, School of Medicine, Dept. of Medicine, *N. 13 Unit 8, Kika-ku, Sapporo 060, Hokkaido, Japan*

A high incidence of lung cancer among chromate workers in Japan has been reported. The chromium content of the lungs of eight patients who had undergone surgery or been autopsied has been measured. A very much higher concentration of chromium was found compared to control lungs. The concentration of chromium was related to the working history (Thorax 33(3), 372-74,1978). The relationship between lung cancer incidence and work place within the chromate industry is now being investigated. Animal experiments administering chromate compounds intratracheally are under way.

143. CANCER RISK IN NON-FERROUS METALLURGY AND CHROMIUM INDUSTRIES

Gabor, S. I., Nagy, L., Popovici, A., Ghelberg, N., Coldea, V., Kovats, A., Valentini, E., Ciontea, G., Modorcea, V., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Health, *Pasteur 6, 3400 Cluj Napoca, Romania*

The summary for this project is under entry no. 97.

144. CANCER INCIDENCE AMONG FERROCHROMIUM AND FERROSILICON WORKERS

Langard, S., Andersen, A., Gylseth, B., Telemark Sentralsjukehus, Dept. of Occupational Medicine, *Olavsgt. 26, 3900 Porsgrunn, Norway*

The aim is to evaluate whether workers exposed to trivalent chromium have an increased risk of developing lung cancer or cancer at other sites by means of a historical study carried out on a population producing ferrosilicon and ferrochromium from 1928. The whole study population includes 976 members of whom 325 are characterized as belonging to a ferrochromium subpopulation. The internal reference population is comprised of workers who have not been exposed at the ferrochromium furnaces. The mortality and cancer incidence in the population is followed from 1935 through 1977. A complete working history of all members of the population is recorded, and an industrial hygiene survey performed. The mortality is compared to that for similar age-groups in the Norwegian population and incidence rates are compared with those for both the total Norwegian population, a local population and an internal population.

145. LUNG CANCER MORBIDITY IN WORKERS EXPOSED TO INDUSTRIAL CHEMICALS

Maties, R., Modorcea, V., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Medicine, *Strada Biserica Amzei 29, Bucharest, Romania*

The summary for this project is under entry no. 30.

146. COHORT STUDY OF CHROMIUM-EXPOSED WORKERS

Puntoni, R., Vercelli, M., Valerio, F., Santi, L. I., Universita degli Studi di Genova, Inst. de Oncologia, Dept. of Epidemiology, *Viale Benedetto 15, Pad. B, 16132 Genoa, Italy*

In the Liguria region there is a factory that produces both hexavalent and trivalent chromium salts. The workers in the factory are exposed to large doses of chromium. An investigation of the causes of death among about 1,300 workers employed in the period 1 January 1958 to 1 January 1978 is being undertaken. The expected deaths will be calculated on the basis of the death rates for the people living in the two villages surrounding the factory.

147. MORTALITY STUDY OF WORKERS IN THE CHROME PIGMENT INDUSTRY

Davies, J. M., Inst. of Cancer Research, Division of Epidemiology, *Clifton Ave., Sutton SM2 5PX, England, United Kingdom*

This is an ongoing mortality study of about 1,000 past and present workers at three English factories where lead chromate and zinc chromate pigments have been manufactured. The main purpose is to ascertain whether the workers have suffered excess mortality from respiratory cancer and the basic results have been published. Deaths from other causes are being studied, and mortality will continue to be monitored.

148. PROSPECTIVE STUDY ON LUNG CANCER IN CHROMIUM PLATING WORKERS

Tsuchiya, K., Okubo, T., University of Occupational & Environmental Health, *Yawata Nishi-Ku, Ooaza-Honjo, Kitakyushu 807, Kyushu, Japan*

In a retrospective study (Keio J. Med.) on chromium platers, the authors did not find an increased risk of lung cancer or of cancers of other sites. In order to confirm this finding, a prospective study on the same population is being peformed, which will require at least five years of observation.

D. OTHER SPECIFIC OCCUPATIONS

149. BLADDER CANCER AND THE PRINTING INDUSTRY - AN HISTORICAL PROSPECTIVE MORTALITY STUDY OF THE PRINTING INDUSTRY

Leon, D., Beral, V., University of London, London School of Hygiene & Tropical Medicine, Dept. of Epidemiology, *Keppel St., London WC1E 7HT, England, United Kingdom*

OBJECTIVE: To investigate whether print workers have an increased risk of dying from cancer of various sites, especially bladder cancer, compared to members of the general population.

APPROACH: The study is of a prospective kind. Approximately 7-9000 print workers who were employed in the industry in a variety of occupations between 1949 and 1963 are being identified from the membership records of two printing trade unions. It will then be ascertained, with the assistance of the Office of Population Censuses and Surveys, whether any of them have since died and if so their cause and date of death.

Sex, date of birth, details of occupation on entry into the union, major occupation changes subsequent to entry while remaining in the union, duration and period of union and branch membership, firm on entry into branch and other relevant information is also being collected from union records. On the basis of this information the risks of dying from various causes within the different occupational groups will be examined and compared. Duration of 'exposure', measured in terms of length of full membership, will also be examined in relation to risk, to see if any dose-response type relationships can be established.

If a significantly increased risk is found for cancer of the bladder, or any other site, the analysis of the deaths from that cause may be extended by carrying out a case-control study. This would allow a more detailed examination of the relationship between type and duration of exposure to risk.

150. MORT/IH STUDY OF WORKERS IN COAL FIRED POWER PLANTS - TVA - EPA

Ortmeyer, C., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Respiratory Disease Studies, *944 Chestnut Ridge Rd., Morgantown, West Virginia,* 26505, United States of America

Pulmonary disease and impairment such as airway obstructive diseases and pneumoconiotic lesions, could arise in part from exposures to gases emitted during coal combustion and to coal dust when coal is burned as fuel for steam-powered electricity generating plants. Those workers who handled the asbestos sheets used to insulate steam pipes may also show evidence of health damage - asbestosis or malignancies. In order to con-

duct research on occupational safety and health problems of TVA employees a memorandum of understanding between NIOSH and TVA was signed in 1976 specifying overall responsibilities for cooperative studies.

Sub-Agreement I, under this memorandum established industrial hygiene studies of workers in coal-fired power plants. The TVA will conduct detailed cross-sectional industrial hygiene studies of workers in selected occupations. Existing industrial hygiene data on past exposures, along with information on control methods will be reviewed in order to retrospectively estimate cumulative working lifetime exposures in occupations where there has been exposure to the same particulates or gases. This information will be used to attempt dose assessment for mortality studies of workers exposed to the same pollutants in the past. The Environmental Investigations Branch will monitor all stages of this study.

Sub-Agreement II, Epidemiological Mortality Study of TVA Employees, is being carried out to estimate the effects in terms of higher-than-expected death rates and/or early retirement due to disability involving principally cardiopulmonary disease or specific malignancies linked to earlier exposures to air contaminants in the workplace environment. All permanent male employees of the TVA with 5 or more years of employment (at least 2 of those years consecutive), and employed sometime between 1-1-55 and 12-31-72 will be included in the cohort for the study.

Required demographic data (age, sex, etc.), most recent and previous addresses, detailed work histories within TVA, and information about dates and causes of death or of early retirement will be obtained. The TVA will assemble and computerize all data from TVA record files for both active and retired employees from the earliest work histories through 12-31-77. (Text Abridged.)

151. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF LEATHER INDUSTRY WORKERS - NCI

Stern, F., Brown, D., Fajen, J., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

Several case-control studies have indicated that individuals employed in the leather industry may experience an excess risk of developing bladder cancer. Cole, in a case-control study, found that leather workers had a relative risk of 2 for developing bladder cancer when compared with a group of matched controls. Another case-control study conducted on all bladder cancer cases referred to the Roswell Memorial Park Research Institute, found a relative risk for bladder cancer of 12.94 for persons employed at least 5 years in the leather industry.

In an attempt to gain additional insight into the relationship between bladder cancer and the leather and leather products industry, mortality rates for bladder cancer were examined in those U.S. countries where the leather industry comprised at least 5 percent of the total employment of the country. Twenty-four counties in six states met these criteria. A definite pattern of increased bladder cancer was found in the 'leather counties' in New England and New York State, however, no unusual risks were found in the 'leather counties' of Pennsylvania and Tennessee. It should be noted that the leather industry in Pennsylvania and Tennessee consisted mostly of small-scale operations of the shoemaker-repairer trade, whereas the leather industry in New York and New England was mainly leather tanneries.

Leathermakers are potentially exposed to chromates, benzidine-based azo dyes and numerous other suspect carcinogens. In addition, NIOSH has recently detected environmental levels of dimethylnitrosamine in a leather tannery. Dimethylnitrosamine has been demonstrated to be an extremely potent carcinogen in numerous animal studies.

A cohort mortality/industrial hygiene study will be conducted to further evaluate the above-mentioned excess risk data. The first phase of the investigation will be a feasibility study to determine the extent of exposure, to characterize the work environment and to assess the feasibility of conducting the mortality portion of the study.

152. MORTALITY STUDY OF WORKERS IN THE NORTHWEST PAPER, PULP AND PLYWOOD INDUSTRY - NCI

Robinson, C., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

The purpose of this project is to follow up on leads supplied by state and national mortality statistics which indicate excess cancer among workers in the wood processing industries. Via contract, a retrospective cohort mortality study of workers in the Northwest paper, plywood and pulp industries will be conducted.

Recent mortality studies conducted by Samual Milham, Jr., M.D., show an excess of lymphatic and hematopoietic cancers in wood processing industry employees. Data developed under NIOSH Contract no. DC-99-74-26 entitled 'Occupational Mortality in Washington State, 1950-71' suggests that persons working in the plywood, paper and pulp industries may be at particular risk. Under this project the contractor will substantiate and refine the earlier occupational mortality findings. An effort will be made to localize any excess mortality within selected plants and to identify agents and processes associated with the increased mortality. The contractor will develop general historical environmental descriptions for each plant. In depth industrial hygiene surveys may be conducted if any excess mortality is observed.

The contract was awarded to Stanford Research Institute. Nine plants were selected for study including four plywood mills and five pulp and paper mills. Data on the study population has been collected, coded, and keypunched. After the data is edited and follow-up is completed, NIOSH will begin analyses of the mortality patterns of the study population.

153. COHORT STUDY OF AUTOMOTIVE WOOD DIE AND MODEL MAKERS

Robinson, C., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

A PRM study conducted by NIOSH on 1257 deceased benefit-eligible members of the National Pattern Makers' League has shown significant proportionate excesses of deaths due to colon cancer and brain tumors. When divided by local leagues into wood shops and metal shops, wood shop pattern makers were observed to have a significant excess proportion of deaths due to leukemia. Non-significant excesses of cancer deaths were found at a number of other sites. Two other studies conducted independently by Sloan-Kettering Cancer Institute and Michigan Cancer Foundation have also shown significantly increased mortality from colo-rectal cancer, as well as elevated bladder and lung cancer rates in subgroups of the study population. Taken together, these three studies suggest increased cancer association with this occupation.

To further investigate these findings, a retrospective cohort mortality study and an environmental assessment are being conducted of about 2000 automotive wood die and model makers who were ever employed at Chrysler, Ford, and General Motors in 1940-1978. The cause-specific mortality of these workers will be compared with that of the general U.S. population. Any unusual patterns of mortality will be examined carefully considering employment work history data and environmental sampling data in an effort to untangle some of the exposures in an environment which includes exposures to wood and plastic dusts, glues, epoxy resins, and solvents.

An industrial hygiene characterization of the model shops was initiated in FY 80. Workers' exposures to total and respirable wood dust, solvents, and amines were measured. These surveys will be completed in FY 81. Surveys will include GM Fisher Body plant, Ford Body Engineering, Chrysler Highland Park, and four job shops represented by the Warren Association.

154. INCIDENCE OF ADENOCARCINOMA OF THE NOSE AND PARANASAL SINUSES AMONG LEATHER AND WOOD WORKERS IN FLORENCE COUNTY (1963-1799)

Cecchi, F., Buiatti, E., Geddes, M., Tomassini, A., Santucci, M., Kriebel, D., Centro Malattie Sociali, *Viale Alessandro Volta, 171 Florence, Italy*

Records of all cases of cancer of the nose and paranasal sinuses which occurred in the period 1963-1977 in the Institute of Radiology and ORL Clinic of the University of Florence were collected. Among 63 cases, 12 adenocarcinomas were found (11 men and 1 woman).

Appropriately matched controls were chosen and detailed occupational histories of cases and controls are being collected by personal interviews. The aim of the study is to confirm previous reports on the association between nasal and parnasal adenocarcinoma and exposure to wood and leather dust. In the county, a considerable number of workers are employed in these industries and their number has in the last decade almost doubled. It seems therefore very interesting to define this specific risk of cancer among them. An epidemiological approach is the first step towards the assessment of the risk and the future protection of the workers.

155. WOOD WORKERS AND CANCER

Esping, B., Axelson, O., University of Linkoping, University Hospital, Dept. of Occupational Medicine, *58185 Linkoping, Sweden*

An excessive incidence of cancer of the nose has been found among wood workers. There are also some indications of an excessive incidence of malignancies elsewhere, but few systematic studies are available. Malignancies of other sites, particularly of the respiratory system, will, therefore, be studied to examine the possible relationship to wood dust exposure. Both the case-control and the cohort approach will be applied in two studies. Various types of wood will be studied with regard to their potential cancer producing properties.

156. STUDY OF WOODWORKERS IN FURNITURE INDUSTRY - A HIGH RISK GROUP FOR ADENOCARCINOMA OF SINUSES

Hadfield, E. H., Macbeth, R. G., Wycombe General Hospital, *High Wycombe, England, United Kingdom*

The high risk group of woodworkers in furniture industry is examined annually (at the workers' work place) by R.G. Macbeth. When some clinical change is visible in their noses they are sent to E.H. Hadfield at the hospital for biopsy and/or treatment.

157. CANCER INCIDENCE AMONG 10,000 NEW MEMBERS OF THE CARPENTERS AND CABINET MAKERS' TRADE UNION

Olsen, J., Sabroe, S., Odense Universitet, Inst. of Hygiene & Social Medicine, Dept. of Social Medicine, *Winslowsvej 17, 5000 Odense, Denmark*

The purpose of this cohort study is to study cancer incidence and all causes of death in 10,000 new Union members and the association between occupational exposures and mortality. Data on cancer morbidity in the members of this cohort will be obtained from the Danish Cancer Register.

158. HEALTH OF FORMER THORIUM WORKERS

Polednak, A. P., Brues, A. M., Rowland, R. E., Stehney, A. F., Argonne National Lab., Division of Biological & Medical Research, *9700 S. Cass Ave., Argonne, Illinois*, 60439, United States of America

The study population is comprised of about 4000 persons (mostly males) who worked at a thorium processing plant from the mid 1930's until 1973. Mortality and causes of death (from death certificates) are being studied with internal comparisons (by job classification and length of employment) and external comparisons (using U.S. mortality rates specific for sex, age, time and cause). For morbidity studies, a subgroup of 558 males (who worked for one year or longer in jobs probably involving highest exposure levels to thorium) has been selected, and questionnaires on medical and occupational history, respiratory symptoms and personal habits (smoking and alcohol consumption) have been sent to those not known to be dead. A random sample of 100 of these 558 men has been selected for a pilot study which involves measurement of radioactivity levels, and a medical examination (including pulmonary function tests). Interest in the health of thorium workers stems mainly from the potential importance of thorium as an energy source. Lung cancer and other lung diseases (e.g., pneumonoconiosis) are of particular interest in these studies, since the major hazard involved in the thorium extraction process is believed to be related to inhalation of airborne thorium and thorium daughter products.

159. EPIDEMIOLOGICAL ANALYSIS OF EFFECTS OF RADIUM

Rowland, R. E., Stehney, A. F., Chalfen, M. H., Argonne National Lab., Radiological & Environmental Research Division, *9700 S. Cass Ave., Argonne, Illinois*, 60439, United States of America

Epidemiological studies are being conducted in order to determine the health effects of exposure to radium. Persons exposed to radium in various parts of the United States are being traced from records of radium dial companies and from other sources. Follow-up of persons located includes determination of vital status and analysis of causes of death (obtained from death certificates) for all, and medical examination, measurements of body radioactivity, and analysis of autopsy reports or materials for part of the group. Analyses of morbidity and mortality are made within the group in relation to body burden of radium. Dose-response patterns are being determined for bone sarcomas with reference to bone sarcomas and carcinomas of the mastoids and the paranasal sinuses. Further analyses will involve other diseases. Mortality and morbidity in specific subgroups of radium cases (e.g., radium dial workers ascertained from employment lists) are being compared with U.S. statistics, with consideration of sex, and other demographic characteristics. At present, about 2,000 persons have been located and measured for radioactivity. Studies of the health of the offspring of certain groups (i.e., female radium dial workers) are also planned.

160. HEALTH STUDY OF PLUTONIUM WORKERS

Voelz, G. L., Stebbings, J. H., Hempelmann, L. H., University of California, Central Office, U.S. Dept. of Energy Los Alamos Scientific Lab., Health Division, *P.O. Box 1663, Los Alamos, New Mexico*, 87545, United States of America

Past and present plutonium workers from six major United States nuclear installations will be followed to determine age-specific mortality rates from all major causes of death, with special emphasis on cancer. Dose-response relationships will be estimated using systemic body burden data from urine tests. The study population, approximately 20,000 individuals, will include all workers with estimated body burdens above one nanocurie, exposed workers with lesser or no body burdens, and random samples of non-exposed workers from the same installations. A cancer incidence study will be undertaken upon a subset of the study population; questionnaire studies of cardiovascular and chronic respiratory morbidity will also be carried out in that subgroup.

161. LIFETIME HEALTH AND MORTALITY EXPERIENCE OF DEPARTMENT OF ENERGY CONTRACTOR EMPLOYEES WITH OCCUPATIONAL RADIATION EXPOSURE

Gilbert, E. S., Marks, S., Breitenstein, B. D., Hanford Environmental Health Foundation Inc., *P.O. Box 100, Richland, Washington*, 99352, United States of America

The objectives of this study are to determine whether adverse health effects of exposure to radiation or other agents or substances may be demonstrated in the Hanford employee population, and, if demonstrated, to establish the nature of the effects.

This research program is a joint effort of the Hanford Environmental Health Foundation (HEHF) and the Pacific Northwest Laboratory (PNL). Over-all planning, design of the system of data collection, planning of the analysis of data and publication of reports are conducted jointly. The collection and processing of data on groups in the worker population, the ascertainment of life status through the Social Security Administration (SSA), and the procurement and coding of death certificates are the responsibility of HEHF. In the latter functions, HEHF may utilize the services of support groups at Oak Ridge

Associated Universities. PNL carries out the analysis of the data.

Seven major files are maintained, containing personnel data, work history, external and internal radiation exposure, exposure to other agents (to the limited extent available), medical history, including laboratory and X-ray data, and mortality data for the deceased in the employee roster. Information in the files dates from the onset of plant operation in 1944 and has been accumulated and refined since 1964. During that period current data have been added to the historical files. Input is provided from personnel and accounting records, radiation monitoring systems, medical questionnaires, physical examinations, laboratory tests and the output of runs of personnel rosters through SSA with subsequent procurement of death certificates. Suitable error routines are used in the processing of the data, and provisions are made for confidentiality of the files of identified data.

Results of the analyses include the demonstration of a more marked healthy worker effect in long-term than short-term workers. Analyses of the relationship of radiation to mortality have disclosed no evidence of a positive trend of mortality with increasing radiation dose for all causes of death or for all cancer. A statistically significant trend has been observed for multiple myeloma and a questionable positive trend for cancer of the pancreas. No correlations are observed for myeloid leukemia or lung cancer. (Text Abridged.)

162. MULTIPLE MYELOMA AND BRAIN TUMORS IN PHYSICIANS

Matanoski, G. M., Diamond, E. L., Elliott, E. A., Johns Hopkins University, School of Hygiene & Public Health, Dept. of Epidemiology, *615 N. Wolfe St., Baltimore, Maryland,* 21205, United States of America

Studying the etiology of these two cancers and their correlation in physicians, a relatively homogenous population which is unique in having a high probability of exposure to repeated low-dose radiation and infections and good medical histories. The design is a case-control study with controls comparable by age, race, sex, and year of death selected from total physician deaths over fifteen years. An equal number of living controls will also be selected. Risk factors identified in previous studies will be examined by telephone interviews with next-of-kin, physicians associates, or physicians if a case-control. There will be special emphasis on determining the exact number of years of exposure to radiation and the estimated dose levels by year or dosimetry data. Questions concerning patient contacts, personal characteristics and medical history will be included. Information on residence, type of training and speciality are available from AMA records. A multi-variate analysis of data will be used to determine association of each of these cancers with radiation, infection, or other factors.

163. MORTALITY SURVEY OF CEGB RADIATION WORKERS AND EX-WORKERS

Harte, G. A., Wheatley, B. M., Bonnell, J. A., Central Electricity Generating Board, Health Physics Research Section, *Berkeley GL13 9PB, Glos., England, United Kingdom*

The objective of the study is to determine whether exposure to low levels of ionizing radiation affects cause of death - in particular whether cancer mortality is higher in people occupationally exposed. Data is to be collected initially on 5,000-6,000 ex-workers, but eventually the study will be extended to current radiation workers (marking about 12,000 in all) and the survey will then run continuously. The exposed population will be compared with the general population, the working population, and eventually it is hoped, control groups within the electricity supply industry.

164. INTERNATIONAL HISTORICAL PROSPECTIVE STUDY OF HEALTH EFFECTS OF MAN-MADE MINERAL FIBRES IN THE PRODUCER INDUSTRY

Saracci, R., Milne, H. E., Jensen, O. M., Teppo, L., Pedersen, E., Westerholm, P., Dodgson, J., Wagner, J. C., Acheson, D., Frentzel Beyme, R. R., Centre International de Recherche sur le Cancer, Epidemiology & Biostatistics Unit, *150 Cours Albert Thomas, 69372 Lyon Cedex 2, France*

The objective of the study is to determine the mortality experience and, whenever possible, the cancer incidence of workers in the man-made mineral fibre (MMMF) production industry. Starting in 1976, factories belonging to the European groups of MMMF manufacturers (CIRFS-EURIMA) were individually visited to identify plants suitable for a historical prospective study, according to the following criteria: (1) No loss or destruction of personnel records; (2) MMMF production process in operation for at least twenty years; (3) some method of mortality/morbidity follow-up available; (4) nominal fibre-size of some fibres less than five microns. On this basis 13 plants, located in seven countries, were selected for study and data collection at these plants, in which workers exposed to MMMF total approximately 4,500, is starting in 1978. Environmental measurements of airborne MMMF concentrations are being carried out in parallel by a team from the Institute of Occupational Medicine, Edinburgh, U.K. Follow-up of the workers will be the responsibility of national collaborating institutions, and comparisons are to be made between groups of workers with various levels of exposure and between worker populations and general (national or regional) populations. All data will be finally submitted to a central, common analysis.

165. MORTALITY STUDY OF GLASS FIBER WORKERS

Shannon, H. S., Muir, D. C., Julian, J. A., Wells, A. R., McMaster University, Occupational Health Program, *1200 Main St. W., Hamilton, Ontario,* L8S 4L8, Canada

A historical follow-up study is being conducted of 3,000-4,000 individuals who have worked in the manufacture of glass fiber since 1948. Mortality will be determined and certified causes of death found. Death rates will be compared internally (with rates in the provincial and national populations) and SMRs will be calculated. Of particular interest will be any deaths due to mesothelioma or lung cancer.

166. IDENTIFICATION OF OCCUPATIONAL RISK FOR COLORECTAL CANCER

Vobecky, J. M., Devroede, G., Universite de Sherbrooke, Faculte de Medecine, Dept. des Sciences de la Sante Communautaire, *c/o Centre Hospitalier Univ., Sherbrooke, Quebec,* J1H 5N4, Canada

A cluster of five cases of cancer of the large intestine has been observed. The patients had several features in common, including work in the same department of a textile plant. By examining the frequency of colorectal cancer in the population, on the one hand, and these common features, in particular the same long term occupational exposure, on the other, the study attempted to determine whether this clustering was only due to chance or to occupational exposure. A study was done on occupational history, familial history of cancer, bowel habits, precursor diseases, and predisposing conditions for all colorectal cancer patients contracting the disease from 1965 to 1976, in the area where the plant is located and in the neighboring areas. Results, based on 1,600 colorectal cancer cases, show that colorectal cancer was 10 times more frequent among synthetic textile workers than in the non-exposed population (Gastroenterology, 75, 221, 1978). In order to establish the etiological nature of this association, a case-control study has been undertaken. The control groups include patients with cancer other than colorectal cancer, patients with diseases other than cancer, and matched neighborhood controls. The on-going phase of the work will establish whether or not an elevated risk of colorectal cancer is associated with employment in any particular part of the plant.

167. AN EPIDEMIOLOGICAL STUDY OF LEUKEMIA INDUCED BY EXPOSURE TO DIFFERENT CHEMICALS

Aksoy, M. B., Erdem, S., Koray, D. A., Guencag, D., Istanbul Universitesi, Faculty of Medicine, Internal Clinic, *Bayezit, Istanbul, Turkey*

The summary for this project is under entry no. 28.

168. EPIDEMIOLOGIC STUDY OF WORKERS IN PETROLEUM REFINERIES AND PETROCHEMICAL PLANTS

Waxweiler, R., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

An NCI study examined the cause-specific mortality experience of workers who were active members of Oil, Chemical and Atomic Workers International Union (OCAW) Locals in

Texas at the time of death. Proportional mortality ratios (PMR's) for stomach and brain cancers, for leukemia, and for multiple myeloma were elevated among white males who worked in petroleum refineries and petrochemical plants and were Union members for at least 10 years. In particular, increased relative frequencies of stomach and brain cancer deaths were found among white male members who were employed at a refinery in Port Arthur (Plant A). In addition, PMR's were elevated for lung cancer among non-whites and stomach cancer in both racial groups employed at another refinery in Port Arthur (Plant B).

Observed numbers of deaths from leukemia, and from cancers of the kidney and skin were greater than expected among white males at Plant B, but observed numbers were very small.

A third refinery in Beaumont, Texas, was found to have excessive frequencies of lung and brain cancers among workers. A case-control study will be done as a timely second step to examine excess deaths from certain cancers in greater detail.

Detailed work histories will be obtained from each case and control to determine length of employment in these plants, specific job(s) held, work location(s) within the plants, and any other employment or exposure information that is available.

The case-control study may be followed by a more definitive cohort study.

169. HISTORICAL DATA BASE FOR ONE COMPANY IN THE PETROLEUM INDUSTRY

Alderson, M. R., Inst. of Cancer Research, Division of Epidemiology, *Clifton Ave., Sutton SM2 5PX, England, United Kingdom*

This project will set up a comprehensive file to examine future queries about the influence of work in a particular process upon mortality from specific diseases. Specific job histories will be obtained for all individuals who have worked at two large refineries for more than one year since these refineries were established. A comprehensive job history will be abstracted and the file will accumulate at the same time data on the plants and processes at each of the refineries including designation of the major variation in the raw materials, intermediaries, and products from each process. Individuals leaving the industry will be traced and the intention is to provide death details for all individuals who have died. This file of data will be primarily used as a computer-based retrieval system to check specific queries about health-risks from various processes. The primary approach will be to relate observed mortality to expected mortality taking into account age, sex, calendar period, and location in the country.

170. CANCER INCIDENCE AMONGST PETROCHEMICAL WORKERS IN WARSAW REGION

Wronkowski, Z. L., Romejko, M., Instytut Onkologii im. Marii Sklodowskiej-Curie, Dept. of Cancer Control & Epidemiology, *15 Wawelska St., 00973 Warsaw, Poland*

The purpose of this study is to determine whether incidence of cancer among petrochemical workers differs from the rates in two control groups, i.e., farmers and the general population in the Warsaw region. The population under study consists of all workers of the Petroleum Plant in Plock who started work after January 1, 1965 - approximately 15,000 individuals. A control group of farmers, individually matched by year of birth and sex, will be used. Both groups will be followed up and cancer cases will be ascertained through linkage of records of the study and control groups and those of the Warsaw Tumor Registry. Data on risk factors for study and control groups will be collected. Age, by individual year, sex and site specific cancer incidence rates will be compared with the expected numbers based on incidence rates in the Warsaw region. Man years of exposure will be calculated for specific cohorts by age and sex so that a dose-response relationship may be tested.

171. OCCUPATIONAL MALIGNANCIES AMONG PETROCHEMICAL WORKERS OF ALBERTA

Grace, M. G., Fincham, S., Egedahl, R., Dr. W.W. Cross Cancer Inst., Dept. of Biostatistics, *11560 University Ave., Edmonton, Alberta,* T6G 1Z2, Canada

A study is in progress to demonstrate possible relationships between occupational exposure to toxic substances and cancer incidence, mortality and mortality from all causes in Alberta. Retrospective data are being collected on approximately 4,500 workers occupationally exposed to chemicals, and unexposed control group similar in size and other characteristics. Sources of data are: a self-administered questionnarie, Vital Statistics, the Provincial Cancer Registry and Patient Index system.

172. HEALTH EFFECTS IN THE PETROLEUM INDUSTRY

Alpen, E. L., University of California, Berkeley Campus, Lawrence Berkeley Lab., *Berkeley, California,* 94720, United States of America

The objective of this project is to examine the health effects of emissions from petroleum refineries and related industries in Contra Costa County, California. Our study populations consist of communities adjacent to refineries and workers engaged in the processing and transportation of petroleum and related products. We are using both direct and indirect studies to compare the health status of occupationally and residentially exposed groups and unexposed control populations. The studies are designed to measure various health outcomes: (1) selected causes of mortality by age; (2) cancer incidence; (3) infertility; (4) congenital malformations; (5) low birth weight and other adverse reproductive effects; and (6) adult and childhood morbidity.

173. HEALTH WATCH - THE AUSTRALIAN PETROLEUM INDUSTRY HEALTH SURVEILLANCE PROGRAM

Christie, D. G., Rockett, I. R., Robinson, K., University of Melbourne, Dept. of Community Health, *159 Barry St., Carlton, Victoria 3053, Australia*

OBJECTIVE: To link present exposure to potential work hazard in the oil industry to subsequent cancer morbidity and mortality.

APPROACH: A prospective concurrent study beginning with a baseline cross-sectional prevalence survey of confounding variables (e.g., smoking). Potential exposure will be assessed indirectly by means of the API job classification; job change will be updated and a job profile, expressed in person years, developed. Outcomes are death and cancer morbidity; controls will be internal.

174. MORTALITY STUDY OF INCREASED BRAIN TUMOR INCIDENCE IN TEXAS CITY, TEXAS

Leffingwell, S., Waxweiler, R., Ludwig, H., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

In response to a complaint of alleged excessive brain tumors among employees at the Union Carbide Company of Texas City, Texas, the Houston South Area Office of OSHA launched an investigation in November of 1978. After a careful inquiry, OSHA requested technical assistance from NIOSH in evaluating the problem.

Preliminary data, supplied with aid of the company, local unions, and local physicians and surgeons, show ten cases in which death certificates indicated brain tumor as cause of death. One additional living employee was found to have a brain tumor. The cell types were predominantly glioma or glioblastoma multiforme with one 'meningioma, angioblastic (sarcoma)'. The workforce at the plant presently numbers 2500. Between 7.5 and 10 thousand workers have worked in the plant between 1941, when the plant began operation, and the present.

Present plans call for additional case-finding, case confirmation by pathological review of tissues, a proportional mortality study (as a check of methodology which may be useful elsewhere), a case-control study of brain tumor deaths, and a cohort mortality study. Coding of company records is being completed and the case-control study will begin soon.

175. CASE-CONTROL STUDY AND OPHTHALMOLOGY SURVEY OF PLANT IN CHARLESTON, W. VA. - NCI

Egan, E., Smith, L., Jones, U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

In response to an employee request, NIOSH began an investigation into an alleged cancer hazard at a DuPont chemical plant in Belle, West Virginia. Subsequent to this employee request, NIOSH received a completed report of a DuPont epi-

demiologic study that demonstrated an excess risk of cancer of the eye, kidney and lung among employees at the DuPont Belle plant.

In order to thoroughly investigate the causes of this excess cancer risk identified among employees at the DuPont Belle plant, NIOSH proposed to conduct a cross-section ophthalmologic survey of workers at DuPont Belle plant and a case control study of the eye and kidney cancer cases.

The cross-section ophthalmologic survey was conducted from March 13, 1978, to April 21, 1978. A total of 1153 persons were examined. One additional case of ocular melanoma was discovered in a pensioned employee. A follow-up of persons discovered in the course of the survey to have pigmented lesions of the optic fundus is planned for FY 80.

The work histories of all the eye and kidney cancer cases identified at the DuPont Belle plant will be compared to the work histories of a group of matched controls to determine if the cancer cases worked more frequently than the controls in any specific job areas.

176. PROSPECTIVE AND RETROSPECTIVE COHORT STUDIES OF MORTALITY AND MORBIDITY AMONG SWEDISH CHEMISTRY GRADUATES

Olin, R. G., Unander, B. D., Alvarsson, B., Kungliga Tekniske Hogskolan, Dept. of Safety & Health, *S10044 Stockholm 70, Sweden*

The causes of death among chemists who belonged to a cohort of men who graduated from the School of Chemical Engineering at the Royal Institute of Technology in Stockholm during the years 1930-1960 were studied. The group was followed until the end of 1977. Results to date show a significant increase in cancers, particularly malignant lymphomas and brain and prostate neoplasms in comparison with the causes of death in the general population, as well as in a similar cohort of architects educated at the same school during the same period of time. The study is at present being continued prospectively. The surviving male chemists have been sent a questionnaire concerning exposures and health effects; the participation rate is about 85%.

177. THE EPIDEMIOLOGY OF LEUKEMIA IN RURAL IOWA

Donham, K. J., Burmeister, L. F., Isacson, E. P., University of Iowa, School of Medicine, Dept. of Preventive Medicine & Environmental Health, *Jessup Hall, Iowa City, Iowa*, 52240, United States of America

Unlike most cancers, leukemias occur at elevated rates in rural and farm populations. Previous studies have been unsuccessful in identifying any specific risk factors for leukemia in rural areas or farming.

Using incidence data from the Iowa Cancer Registry, we have completed extensive preliminary ecologic-epidemiologic studies which have indicated there are elevated leukemia rates in Iowa which are strongly associated with: 1) male sex, 2) rural residence, 3) proximity to high cattle population densities, and 4) proximity to dairy herds with cases of bovine lymphosarcoma. The elevated rates and the associations noted were primarily associated with acute lymphoid leukemia (ALL). These preliminary data are suggestive that cattle and perhaps the bovine leukemia virus (BLV) may be factors in the high rates of leukemia seen, at least for ALL. We propose a case-control study to verify the ecologic relationships seen in the preliminary studies, and to investigate on an individual basis the role of various factors in the rural and agricultural environment that may contribute to the observed high leukemia rates.

Approximately 200 cases of ALL (male and female) will be drawn from the Iowa Cancer Registry for the 66 rural counties. Two normal controls for each case will be selected from the same counties, and the cases and controls will be matched for age, sex, and county of residence. Personal interviews of each case and control will be completed to obtain data on: 1) environmental or occupational exposure to cattle, 2) environmental or occupational exposure to bovine leukemia virus, 3) farm or non-farm occupation, and 4) various exposures within farming such as agricultural chemicals and other livestock species.

Dairy herds of cases and controls will be tested serologically to determine the extent of BLV infection. The data will be analyzed to discern a possible cause-effect relationship of exposure to cattle, BLV, and other factors in the rural/agricultural environment.

178. EPIDEMIOLOGICAL STUDY OF CEREBRAL TUMORS IN ADULTS

Burch, J. D., Howe, G. R., Miller, A. B., National Cancer Inst. of Canada, Epidemiology Unit, Dept. of Preventive Medicine & Biostatistics, *12 Queens Pk. Cres. W., c/o University of Toronto, Toronto, Ontario*, M5S 1A8, Canada

Little is known of the etiology of cerebral tumors in humans, although associations have been suggested as a result of incidence, mortality, and animal studies. These include urban/rural differences, occupation with specific reference to farming, the rubber industry, and exposure to vinyl chloride, familial associations, ionizing radiation, brain trauma, and specific chemical carcinogens. The current study will re-investigate these associations and explore other possible relevant factors. The study will test the hypotheses that cerebral tumors are associated with specific occupations (farming, rubber industry, plastics industry), family history of brain tumor, and exposure to nitrosamines, especially through drinking water and preservative-containing meats and meat products. A number of questions will also be asked of respondents relating to additional environmental factors (e.g., smoking, alcohol consumption, etc.). Data on past events and exposures will be obtained from cases and hospital controls through personal interviews in the respondents' homes using proxy respondents for dead or incapacitated cases and appropriate proxy controls. Case and control acquisition is restricted to the metropolitan Toronto and fringe areas and will include incident cases with defined histology for the four-year period 1 January 1977 to 31 December 1980.

179. MORTALITY AND INDUSTRIAL HYGIENE STUDY OF PHOSPHATE WORKERS

Herrick, R., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

NIOSH is conducting an epidemiological study of mortality patterns among phosphate (fertilizer) production workers. Interest in the chronic health effects associated with this industry developed because of three observed cases of lung cancer in phosphate production workers, all reported to be non-smokers. The hypothesis of an association between lung cancer and phosphate exposure seems to be supported by studies by other Federal agencies and the Florida State Department of Health, which have suggested an increased rate of lung cancer among the county populations surrounding the phosphate plants. This study involves: (1) industrial hygiene evaluations at a number of phosphate mining and phosphate fertilizer plants, (2) a retrospective cohort study of phosphate fertilizer workers' mortality patterns, and (3) a case-control study on the same population in the cohort study to determine if the risk of lung cancer is associated with employment in specific job categories. The facility chosen for study currently employs over 500 people, and has employed approximately 4,000 people since the start up of plant operations in 1951. The overall industrial hygiene report will be finalized in 1980. At that time it will be determined if any additional industrial hygiene monitoring is needed. Follow-up will continue for cohort study members until the vital status of approximately 95 percent has beed determined. When this is accomplished, analyses can be done for the retrospective study and cases and controls can be chosen for the subsequent epidemiological study.

180. STUDY OF FERTILIZER MANUFACTURERS

Fraser, P. M., Chilvers, C. E., Beral, V. S., Fox, J. W., Hill, M. J., University of London, London School of Hygiene & Tropical Medicine, Dept. of Epidemiology & Medical Statistics, *Keppel St., London WC1E 7HT, England, United Kingdom*

The hypothesis that high nitrate ingestion causes cancer is being examined in workers exposed to nitrate-containing dust in the manufacture of fertilizer. A census-based study links occupational data from the 1961 and 1971 censuses of England and Wales to mortality data from the National Health Service Central Register.

181. PESTICIDE MANUFACTURER/FORMULATOR MORTALITY STUDY

Carnow, B. W., Epstein, S. S., Levy, P., DiTraglia, D. P., University of Illinois, Medical Center at Chicago, School of Public Health, Dept. of Occupational & Environmental Medicine, *Box 4348, Chicago, Illinois*, 60680, United States of America

This study is seeking to determine if selected groups of workers in the pesticide manufacturing/formulating industry experience excess cause-specific mortality. Although a number of epidemiological studies have been carried out to examine the relationships between chronic pesticide exposure and morbidity and mortality, most have not included sufficient population numbers, length of exposure and latency periods in the study design. A cohort of approximately 4,000 workers who were employed in the pesticide manufacturing/formulating industry for a minimum of 12 months prior to 1960 will be studied and their mortality experience will be compared to that of the general population for 60 causes of death. In addition, attention will be directed to various categories of malignant and non-malignant lesions specifically associated with exposure to organochlorine pesticides. A prospective cohort of workers in the pesticide industry will also be identified.

182. EPIDEMIOLOGICAL STUDY OF CANCER MORTALITY IN AN AREA WITH INTENSIVE USE OF PESTICIDES IN GREENHOUSES

Buiatti, E., Cecchi, F., Geddes, M., Tomassini, A., Marchi, M., Vigotti, M. A., Centro Malattie Sociali, *Viale Alessandro Volta, 171 Florence, Italy*

A multidisciplinary research has been started in the town of Pescia (Tuscany), in which the prevailing occupation is represented by flower production in greenhouses, and the amount per acre of pesticides used is very high.

The aim of the epidemiological research is to evaluate a possible difference in cancer death rate between the area of Pescia and a control area nearby in which the prevailing occupations are related to tourism.

A study of the frequency of malformations will be carried out in parallel.

In the meantime, other research groups will study a series of parameters of environmental pollution; the possibility of alternative pest control practices will also be evaluated.

183. MORTALITY AMONG FOREST WORKERS

Axelson, O., Granstam, S., Edling, C., University of Linkoping, University Hospital, Dept. of Occupational Medicine, *58185 Linkoping, Sweden*

Several studies have shown an increased risk of cancer among people with exposure to various herbicides. Forest workers in Sweden have used phenoxy acids since the beginning of the 1950s and an evaluation of the mortality pattern might show particular features. The study will be descriptive in character and will show the proportional mortality for various causes of death. About 1,030 forest workers are known to have died during the study period, 1968-1977, as recorded on union registers. Using case-control techniques, a second part of the study will examine cause-effect relationships between cancer and exposure to phenoxy acids.

184. MORTALITY ANALYSIS OF UNITED AUTO WORKERS COHORTS

Whalen, J., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Exposure to known or strongly suspected carcinogens (e.g., asbestos, chromate pigments and plating solutions, coke oven emissions, cutting fluids, etc.) has been documented for workers in the automobile industry as well as in related industries such as metal working. Recently, studies have indicated increased proportions and rates of cancer deaths among workers in these industries. Most of these studies have been of a preliminary nature, and additional epidemiology studies are required to further define any hazards which may exist in these industries.

A preliminary evaluation of the United Auto Workers International Union's (UAW) computerized central pension files, as well as membership and seniority records, indicates that this data base is adequate to conduct epidemiology studies of disease excess and disease etiology in the union membership. Therefore, when considering the uniqueness of this data base, a contract will be awarded to UAW to conduct studies of occupational cancer epidemiology. In addition to providing epidemiology studies of the automobile and related industries, it is hoped this project will serve as a model for self-analysis by other large labor unions.

185. MORTALITY STUDY OF STEEL WORKERS

Nakamura, K., National Inst. of Industrial Health, Dept. of Industrial Epidemiology, *2051 Kizuki Sumiyosityo, Kawasaki, Kanagawa, Japan*

Excesses of respiratory cancer among coke oven workers are considered to be related to the exposure to coal tar effluents. To study whether there are any other carcinogenic risk factors in the environment of iron and steel producing plants, about 300,000 steel workers who had worked for at least 1 year at the beginning of 1973 in one of 127 plants in Japan were registered as members of the study cohort. Ascertainment of deaths will be obtained from the family registry system in Japan and death certificate information will be collected from the District Legal Affairs Bureau. In a preliminary stage, the cohort will be followed up retrospectively to the end of 1976, but follow-up thereafter will be continued.

186. MORTALITY STUDY OF FOUNDRY WORKERS

Duncan, K. P., Health & Safety Center, *97 Horseferry Rd., London SW1P 2DY, England, United Kingdom*

This study will investigate the mortality of workers in both iron and non-ferrous foundries. A population of about 1800 men who were employed in foundries in 1963 will be compared to a control population of 1700 men in other factories. The incidence of lung and other cancers as well as non-malignant respiratory disease and other causes of death will be investigated.

187. MORTALITY STUDY OF WORKERS IN TWO SCOTTISH STEEL FOUNDRIES

Duncan, K. P., Health & Safety Center, *97 Horseferry Rd., London SW1P 2DY, England, United Kingdom*

The mortality pattern of workers in two foundries in Scotland will be investigated following the suggestion that atmosphere from the foundries was responsible for an increase in lung cancer in the area. The population will consist of about 4,200 past and present employees of the foundries. Mortality from all causes of death and from lung cancer in particular will be studied.

188. CANCERS AMONG THE FOUNDRY WORKERS IN KAWAGUCHI, SAITAMA

Sasaba, T., Kubo, T., Saitama Cancer Center, Dept. of Epidemiology, *818 Komuro, Ina-Machi, Kitaadachi-Gun, Saitama-Ken 362, Japan*

OBJECTIVE: Positive etiological relationships were reported between pneumoconiosis and exposure to foundry sand. This survey deals with the problem of cancer, especially of lung cancer, among the foundry workers.

APPROACH: Retrospective survey for patients with cancer in the period 1971-1975 was started. Prospective study will be started shortly.

PROGRESS: So far cancer patients for the period 1974 and 1975 have been and are in the process of analysis.

189. MORTALITY OF BRITISH COKE-OVEN WORKERS

Jacobsen, M., Fanning, D. M., Collings, P. L., Archibald, R. M., Hurley, J. F., Inst. of Occupational Medicine, Statistics Branch, *Roxburgh Pl., Edinburgh EH8 9SU, Scotland, United Kingdom*

The objective of this investigation is to estimate death rates from cancers in general and lung cancer in particular among British coke-oven workers. A cohort of men employed in 1967 at industrial establishments involving coking operations is being studied. Men involved are or were employees of the British Steel Corporation or of a subsidiary of the National Coal Board. Analysis of a nine-year follow-up period suggests an occupationally related lung cancer hazard at some works, and that this hazard is considerably smaller than that reported among American coke workers. The study continues.

190. LUNG CANCER MORTALITY IN MEN EXPOSED TO DUST

Haider, M., Neuberger, M., Kundi, M., Gruendorfer, W., Popper, W., Universitat Wien, Inst. of Environmental Hygiene, *Kinderspitalgasse 15, 1090 Vienna, Austria*

1,630 men exposed long-term to dust (foundry workers, workers in metal, ceramics, glass, stone and other industries) and 1,630 non-exposed matched controls were registered betwen the years 1950 and 1960 for a prospective study of workmen living in Vienna, born 1910 or before. In a separate historical cohort study on asbestos cement workers the same methods are used to compare their mortality data with data from a cohort of cement workers from the same region. (Preliminary results were published in 'New approaches to risk estimation of air pollutants', Facultas, Wein, 1979.)

191. MORTALITY AND CANCER DEATH AMONG CHIMNEY SWEEPS

Stoettrup Hansen, E., Kobenhavns Universitet, Faculty of Medicine, Institute of Hygiene, *Blegdamsvej 21, 2100 Copenhagen 0, Denmark*

Among the adverse influences to which chimney sweeps are exposed are excessive heat and significant amounts of chemicals in combustion products; in addition, they are subject to a severe physical strain. A retrospective and prospective cohort study of the mortality pattern and, especially, the incidence of malignant neoplasms among chimney sweeps will be made. The study will include all Danish chimney sweeps (about 700 persons). A preliminary study of the Copenhagen chimney sweeps from 1958 to 1977 indicates that cancer deaths among chimney sweeps aged 40-69 years are 3-4 times as frequent as might be expected. Malignant neoplasms of lymphatic and hematopoietic tissue were found to occur as often as respiratory cancer. Pancreatic cancer, too, constituted a much higher proportion of the cancer deaths than expected. Suggestions of a causal relationship between specific cancer sites and exposure to high temperatures, certain metals and certain volatile hydrocarbons will be investigated. An estimation of present day exposure will be made through examination of the hygiene conditions at the place of work.

192. CANCER INCIDENCE AND MORTALITY AMONG RAILROAD WORKERS

Howe, G. R., Lindsay, J., Miller, A. B., University of Toronto, *Medical Sciences Bldg., Toronto, Ontario*, M5S 1A8, Canada

In a recent case-control study (Tobacco Use, Occupation, Coffee, Various Nutrients, and Bladder Cancer, G.R. Howe et al. JNCI, in press) an association was observed between any occupation related to railroads and increased risk of bladder cancer. The present study is a cohort study using pension records from a large Canadian railroad company. Records from 1965 onwards are being linked using computerized techniques, to the Canadian mortality data base, and records for those from 1969 on are being linked to the Canadian cancer incidence reporting system. Thus mortality between 1965 and 1976, and cancer incidence between 1969 and 1976 can be related to various occupations within the railroad industry.

193. HERBICIDE EXPOSURE AND CANCER INCIDENCE AMONG RAILROAD WORKERS

Axelson, O., Sundell, L., University of Linkoping, University Hospital, Dept. of Occupational Medicine, *58185 Linkoping, Sweden*

An earlier report (Axelson and Sundell, Work Environ Health 11, 21-28, 1974) indicated a cancer hazard due to exposure to amitrole. Further evaluation has shown that exposure to phenoxy acids might also produce cancer (Axelson, Scand. J. Work Environ Health 4,85-89, 1978) and this is confirmed in another recent study on mesenchymal tumors and exposure to phenoxy acids and chlorophenols (Hardell, Laekartidnignen 75, 3535, 1978). It seems pertinent, therefore, to update the earlier study of a cohort of railroad workers to find out whether or not the increased cancer mortality continued after 1972.

194. MORTALITY OF HAIR DYERS AND TINTERS

Alderson, M. R., Inst. of Cancer Research, Division of Epidemiology, *Clifton Ave., Sutton SM2 5PX, England, United Kingdom*

This study will examine the mortality of a group of hair dyers and tinters followed from 1961 to 1976 and compare their causes of death. Census data will be used to identify a sample of all hairdressers throughout England and Wales; the staff from the Office of Population Census and Survey will identify individuals specifically describing themselves as hair dyers and tinters at the time of the census. These individuals will be traced through the National Health Service Central Register and for those that have died the cause of death will be released. The all-cause mortality, mortality from malignant disease and from other diseases will be examined.

195. INCIDENCE OF CANCER AMONG SELECTED GROUPS IN DENMARK

Clemmesen, J., Sorensen, B. L., Finseninstitutet, Danish Cancer Registry, *Strandboulevarden 49, DK2100 Copenhagen, Denmark*

A series of studies of cancer risk in selected groups and occupations is being undertaken. These will include the distribution of cancer among hairdressers, and risk of thyroid cancer among patients with thyroid struma, the geographical distribution of leukaemia and Hodgkin's disease in Denmark and a case-control study of cancer of the bladder.

196. MORTALITY AMONG DRY CLEANERS

Blair, A. E., Decoufle, P. N., Grauman, D. J., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst., *9000 Rockville Pike, Bethesda, Maryland*, 20205, United States of America

Workers in dry cleaning shops are exposed to such chemicals as tetrachloroethylene, trichloroethylene, petroleum solvents, and carbon tetrachloride, some of which are carcinogenic in animals. A cohort follow-up study of 10,000 members of a dry cleaning union between 1940-1977 is being conducted. Cause-specific mortality rates will be compared to expected rates from the general and local populations, and title and duration of membership will provide an indication of exposure gradients and latent periods.

197. MORBIDITY AND INDUSTRIAL HYGIENE STUDY OF FIBROUS MINERAL WORKERS (ATTAPULGITE CLAY)

Cameron, T., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

The two companies which mine and process most of the attapulgite clay in the United States will provide medical data on their 600 workers. One of the companies has medical data covering three years. NIOSH in Cincinnati has already completed an IH survey in one of the mining and milling facilities. The National Cancer Institute will conduct a survey in the other mining and milling facility.

198. CANCER INCIDENCE IN A TELEPHONE WORKER POPULATION

Maruchi, N., Sakai, Y., Nakamura, T., University of Tokyo, Faculty of Medicine, Dept. of Health Administration, *7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Tokyo, Japan*

A retrospective study of incidence and mortality rates of cancer has been carried out for the period of 1971-1976 among the 50,000 employees of a Tokyo telephone and telegram company. Information about sick leave, hospitalization, health checkups, death, etc., has been collected. Should excess risk for any cancer site be detected, the responsible factors will be studied.

199. INCIDENCE OF LEUKEMIA AND LYMPHOMA IN AN EXPLOSIVES FACTORY

Gillis, C. R., Hole, D. J., Greater Glasgow Area Health Board, Cancer Intelligence Unit, *520 Bilsland Dr., c/o Ruchill Hospital, Glasgow G20 9NB, Scotland, United Kingdom*

A cohort of workers at an industrial plant producing explosives has been enumerated. The incidence and mortality of leukaemia and lymphoma amongst the workers in the subsequent ten years is higher than expected when compared with age-matched general population rates over the period. Investigations to identify common features from detailed occupational histories and proximity to potential carcinogenic hazards, fo-

gether with other suspected aetiological factors which occur outside the work environment, are being carried out.

200. CANCER INCIDENCE AMONG CERTAIN GROUPS IN THE ELECTRONIC INDUSTRY

Vagerov, D. H., Allander, E., Olin, R., Huddinge Sjukhus, Dept. of Social Medicine, *S14186 Huddinge, Sweden*

The aim of this study is to examine the incidence and mortality of cancer in a group of workers in the electronic industry, and to investigate the ways in which the medical care organization inside the industry deals with occupational hazards.

E. BROAD EPIDEMIOLOGICAL SURVEYS OF OCCUPATIONAL CARCINOGENESIS

201. EXPOSURE-BASED CASE-CONTROL APPROACH TO DISCOVERING OCCUPATIONAL CARCINOGENS

Siemiatycki, J., Gerin, M., Hubert, J., Thomas, D., Armand Frappier Institut, Centre de recherche en Epidemiologie et Medecine Preventive, *531 Blvd. des Prairies, Case Postale 100, Laval des Rapides, Quebec*, H7N 4Z3, Canada

Of the thousands of chemicals present in the environment, only a few have at present been demonstrated to be human carcinogens. There is no evidence one way or another, regarding human carcinogenesis, for almost all of the others. The discovery of unsuspected hazards is an important public health challenge. The very large number of agents to be considered renders inadequate conventional 'one-factor-at-a-time' epidemiologic study methods. A few methods have been suggested which would have the effect of scanning the occupational environment to detect hitherto unsuspected human carcinogens. Even the most sensitive of these methods suffers from the non-specificity of job titles in ascribing occupational exposures. A case-control-type approach based on exposure histories, and not simply job-title histories, of incident cases and controls incorporates breadth (the entire occupational spectrum), depth (capacity to pinpoint not only high risk occupations but also specific chemicals), and statistical sensitivity. Exposure histories are obtained in a two-stage process. A probing interview is carried out to obtain descriptions of each of the persons' jobs. Based on technical documentation and personal consultations with expert collaborators, engineers and chemists then scrutinize each person's work history and draw up a list of possible chemical exposures. A pilot study has shown the method to be feasible. Eligibility criteria for cases are: male; aged 35-70; diagnosed in any of the 17 major Montreal area hospitals as having cancer of the esophagus, stomach, colon, liver, pancreas, lung, prostate, testis, bladder, kidney, skin melanoma, and lymphoma. Two control series will be used for each site, one selected from cancer patients with other sites and another from the general population. A sub-objective is to compare results obtained using cancer controls with those obtained from population controls. In total, 1500 patients and 200 population controls will have been interviewed. The distribution of chemical exposures among patients having a common tumor is analyzed to estimate the relative risk corresponding to each substance noted in any patient's history. It is anticipated that this method will detect heretofore unsuspected carcinogens.

202. OCCUPATIONAL AND NON-OCCUPATIONAL RISK FACTORS OF SQUAMOUS CELL CARCINOMA OF SKIN IN THE MONTREAL REGION

Aubry, F., McGill University, Dept. of Epidemiology & Health, *3775 University St., Montreal, Quebec*, H3A 2B4, Canada

Data from the Cancer Registry of the Province of Quebec indicate that skin cancer is one of the leading types of cancer in the Montreal region. Given that the two major risk factors of squamous cell carcinoma of the skin recognized in the medical literature are sunlight exposure and the Celtic characteristics of people and that these factors are not particularly marked in the Montreal region, the possibility exists that other risk factors, particularly occupational, could play a role. The objective of this case-control study is to assess the relative risk associated with occupational and non-occupational known and suspected risk factors of squamous cell carcinoma of the skin diagnosed in the Montreal region, specifically occupational exposure to sunlight and/or to chemical agents and radiations. The cases are defined as all cases of squamous cell carcinoma of the skin diagnosed during the two years preceding the beginning of the study in the pathology departments of Montreal hospitals. Two controls matched for sex and age with each case will be selected from among pathology records at the same hospital at which the case was found. The controls will be subjects in whom a pathological diagnosis will have been made for skin condition which is non-malignant and which is not known to be related to the risk factors of squamous cell carcinoma of the skin. Cases of pemphigus vulgaris, bullous pemphigus, intradermal naevus and lichen planus will thus be included. The total number of cases in this study is estimated between 400 and 800. A postal questionnaire on occupation and exposure to environmental factors will be sent to each case and each control and telephone calls will then be made to complete missing information. Data will be analysed by means of a discriminant analysis.

203. MALIGNANT MELANOMA AND ENVIRONMENTAL EXPOSURE

Aldrich, T. E., University of Miami, School of Medicine, Dept. of Epidemiology & Public Health, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida*, 33152, United States of America

This is a non-concurrent, prospective study of environmental exposure to petroleum residues (from conbustion) and the risk of malignant melanomas. Industrial workers considered to be at high risk (e.g., flight line workers, toll booth operators) will be studied in contrast to workers exposed to sunlight (e.g., telephone company employees) or to petroleum residues only (e.g., auto mechanics). Communities in proximity to sources of exposure (e.g., airports, highways) will also be studied, in contrast to communities not so exposed, for melanoma rates. An anticipated 800 persons will be included from industry with an additional study population being the communities studied from institution records only.

204. GEOGRAPHICAL DISTRIBUTION OF MALIGNANT NEOPLASMS OF THE BRAIN IN CANADA

Neutel, I. C., University of Ottawa, Faculty of Medicine, Dept. of Epidemiology & Community Medicine, *1145 Carling Ave., Lady Grey Bldg., Ottawa, Ontario*, K1Z 7K4, Canada

Malignant neoplasms of the brain have received very little epidemiological attention in spite of the low survival rate and their occurrence in childhood or early adulthood. A few studies dealt with their general distribution in the United States and Denmark and only one studied the geographical distribution in relation to environmental factors. This project will study the geographical distribution of brain tumours across Canada using both mortality and incidence data by calculating age-adjusted mortality and incidence rates for census divisions. These rates can be related to various environmental variables known for the census divisions. In addition, this study will investigate the occupations recorded for a selected group of brain tumour deaths and compare them with those of a matched group of controls. Of special interest will be occupations likely to involve chemical or radiation exposure. Prenatal radiation has been shown to increase the risk of childhood cancer of the central nervous system, and the same situation may apply to adult brain cancer.

205. OCCUPATIONAL, ATMOSPHERIC AND DIETARY FACTORS AND HABITS ASSOCIATED WITH EPIDERMOID CARCINOMA OF THE BUCCAL CAVITY IN CHILE

Inzunza Hernandez, O., Cabezas Soriano, J., Majlis Moisseff, G., Hospital Jose Joaquin Aguirre, Asignatura de Fisiopatologia, *Av. Santos Dumont 999, Santiago, Chile*

OBJECTIVE: Information is available in the world literature on factors associated with buccal cancer, such as alcohol and tobacco consumption, diet and other habits. Given the ethnic, geographic, cultural and social differences between Chile and the countries producing this information, we propose to study the factors associated with buccal cancer in this country. The final objective is to apply the information obtained to the diagnosis of a population at high risk of developing buccal cancer and to implement in those persons preventive methods and early diagnosis of the neoplasia. We believe that based upon this analysis we will be able to detect mutagens for further study.

METHODS: 1) Analysis of morbidity and mortality statistics for buccal cancer throughout the country, studying the extent of the sample, distribution by anatomic site, distribution

by geographic site, etc. 2) Analysis of the type of diagnosis, e.g., clinical, radiographic, histopathologic, type of pathology, degree of extension of the lesion, etc. 3) Using records of various treatment centers, compile a list of patients who are alive, who have epidermoid carcinoma of the buccal cavity or premalignant or potentially cancerous lesions. 4) Selection of a control group, two controls per cancer patient, comprised of individuals with the following similar characteristics: race, age, level of education, place of residence, occupation. 5) Interview of patients and controls to include: time of development of the lesion, prior diseases, teething, family history, occupation, place of residence, diet, habits, etc. 6) Tabulation and discussion of results.

PROGRESS: We have completed steps 1 and 2 and we are currently compiling a list of patients with epidermoid carcinoma of the buccal cavity.

206. AN EPIDEMIOLOGICAL STUDY OF STOMACH CANCER IN NORTH STAFFORDSHIRE

Veys, C. A., Cole, R. B., North Staffordshire Medical Inst., Industrial & Community Health Research Centre, *Hartshill, Stoke on Trent ST4 7NY, England, United Kingdom*

The mortality from stomach cancer in Stoke-on-Trent is one of the highest recorded in the United Kingdom, but the reasons for this are unknown. Some positive associations between stomach cancer and occupation have been observed, in particular with certain dusty trades; and there is also an association with suspended particulate air pollution. For many years in the past, the North Staffordshire area has been noted for its high level of air pollution, which was predominantly caused by smoke emission from local major industries, especially pottery manufacture. Coal mining also predominates and there are many other dusty occupations. The main objective of the study, which is in two parts, is to examine whether occupational factors (especially dust exposure) play a part in the aetiology of stomach cancer in the Stoke-on-Trent area. The investigation will encompass firstly a detailed examination (in epidemiological terms) of each case of stomach cancer (both male and female) that occurred in the County Borough District of Stoke-on-Trent within the fifteen year period 1961-1975. In addition, a prospective case-control study on each person newly presenting with stomach cancer within the succeeding three years (beginning in 1977) will be undertaken. A detailed whole life occupational history will be obtained at interview and matched against that obtained from four controls chosen at random from the population at large. The data will be compared and contrasted for statistically significant differences in the dust exposure between cases and control groups.

207. ENVIRONMENTAL RISK FACTORS IN NASOPHARYNGEAL CARCINOMA IN MALAYSIA

Armstrong, R. W., University of Hawaii System, Manoa Campus, School of Arts & Sciences, Dept. of Geography, *2444 Dole St., Honolulu, Hawaii*, 96822, United States of America

The objective of this research is to compare the self-specific environments of Chinese and non-Chinese patients having nasopharyngeal carcinoma (NPC) with those of healthy control subjects to identify particular patient-environment interactions that may play a part in the etiology of NPC. The research will pay particular attention to exposures to certain occupational environments and dietary patterns both of which are suspected, on the basis of previous research, of being associated with a high risk of NPC. The control subjects will be sampled from the general population to serve as comparison groups in the determination of relative risk. Information on the self-specific environments will be collected through structured and non-structured interviews of 110 patients, 160 control subjects and members of their families. Information will also be collected from investigations of job sites, residences, and neighborhoods. The interviews will seek information on the daily activity patterns of the participants spread over one week.

The field work will be conducted in the State of Selangor, Malaysia. The research will clarify evidence for the association between poorer socioeconomic environments and NPC, and test various hypotheses, particularly that carcinogens are inhaled in certain industrial occupational settings, and that exposure to Cantonese salted fish is a high risk NPC factor. The research will also examine the value of using daily activity patterns as a basis for obtaining information about self-specific environments and the importance of this information in identifying possible environmental risk factors. The methodology could have application in studies of other cancers.

208. EPIDEMIOLOGY OF GASTRIC CANCER IN NEWFOUNDLAND

Pfeiffer, C. J., Fordor, J. G., Threlfall, W., Memorial University of Newfoundland, School of Medicine, Laboratory of Investigative Gastroenterology, *Health Science Complex, St. John's, Newfoundland*, A1C 5S7, Canada

The purpose of this epidemiological investigation is to: (1) characterize the demographic and statistical pattern of gastric cancer in Newfoundland by regional analysis and international comparison, (2) determine high and low risk geographical regions and occupations of the male work force, (3) quantitatively study water trace element composition from high- and low-risk sectors, as well as other indicated environmental, or geochemical factors, (4) relate such findings to incidence of cancer of all sites combined and death attributable to all causes, and undertake, on a comparative basis, an analysis of occupational risk and water trace element correlates with gastric cancer in the high and low risk areas of Iceland and Japan. Data from Newfoundland, Iceland and Japan will be analyzed in an identical fashion by stepwise, multivariate analysis. Statistical and chemical analytical work will be conducted in Canada.

209. EPIDEMIOLOGICAL STUDY OF LARYNGEAL CANCER

Miller, A. B., Burch, J. D., Howe, G. R., University of Toronto, *Medical Sciences Bldg., Toronto, Ontario*, M5S 1A8, Canada

The study is designed to investigate the contribution of known and suspected aetiological factors to laryngeal carcinoma. It is hypothesized that there is an association between laryngeal carcinoma and the smoking of tobacco and that there is a reduced risk for smokers of filter cigarettes. It is also proposed that there is a synergistic effect between alcohol consumption and the smoking of tobacco. A further hypothesis is that there is an association between laryngeal cancer and exposure to asbestos in the environment and occupationally, especially for those who smoke cigarettes. It is also hypothesized that there is an association between cancer of the larynx and exposure to nickel refining and processing. The study is a case-control study with data on past events and exposure obtained from cases and controls by means of a detailed questionnaire which is administered personally to cases and controls in their homes. The study population consists of all newly diagnosed cases with carcinoma of the larynx, March 1, 1977, to April 31, 1978, resident in Southern Ontario and the Sudbury, and North Bay areas in Northern Ontario. Controls are matched to cases by age (plus or minus five years), sex, and neighborhood of residence. Controls are obtained by door to door survey. At the end of 16 months of interviewing, a total of 130 case-control pairs have been interviewed. It is anticipated that a total of 200 case-control pairs will be available for analysis.

210. ETIOLOGICAL FACTORS IN CANCER OF UPPER RESPIRATORY AND DIGESTIVE TRACTS

Brugere, J., Point, D. D., Bataini, P. G., Fondation Curie, Service de Chirurgie Cervico-Faciale et ORL, *11 rue Pierre et Marie Curie, 75231 Paris Cedex 5, France*

Four main groups of neoplasms (oral cavity, oropharynx, larynx and hypopharynx) are being analyzed. A comparative study is carried out with special reference to occupation, dental status, smoking and drinking habits, precancerous lesions, sex and age. This information will be compared for the four groups and for ENT Department outpatients without evidence of neoplasm.

211. OCCUPATION AND NASAL CANCER

Engzell, U. K., Englund, A., Westerholm, P., Nordlinder, H., Lindgren, A., Hernberg, S., Schultz Larsen, D., Sand Hansen, H., Huddinge Sjukhus, Dept. of Ear, Nose & Throat, *S14186 Huddinge, Sweden*

An increased frequency of cancer of the nose and paranasal sinus among workers exposed to fine wood dust, leather and nickel has been reported from England and other countries. A joint project has been started to explore the risk of contracting nasal cancer in the Nordic countries and to single out occupa-

tions and exposures possibly associated with nasal cancer. In each country a project group is at work on a national basis, according to a joint program. Each new case of malignant epithelial tumor of the nose and sinuses reported to the individual national cancer registries is interviewed concerning previous occupational exposures of various kinds. There are an estimated 150 cases a year. The project is a case-referent study and the controls will be matched cases of colon cancer.

212. STUDY OF OCCUPATIONAL FACTORS IN NASAL SINUS CARCINOMA

Elwood, J. M., Cancer Control Agency of British Columbia, Division of Epidemiology, *2656 Heather St., Vancouver, British Columbia*, V5Z 3J3, Canada

Since 1938, approximately 125 male patients with nasal sinus carcinoma have been identified in the major treatment facility in British Columbia. Information on the occupation of these patients, and on certain other factors, such as ethnic origin and smoking history, is being collected from medical records and compared to census data on occupations, and also to similar data on a controlled series of other cancer patients matched by age and year of diagnosis. The analysis will assess the associations of risk of nasal sinus cancer with specific occupations.

213. CASE-CONTROL STUDY ON THE OCCUPATIONAL AETIOLOGY OF PARANASAL SINUS CANCER

Hernberg, S. G., Linderborg, H. N., Tola, S. A., Inst. of Occupational Health, Dept. of Epidemiology & Biometry, *Haartmaninkatu 1, SF00290 Helsinki 29, Finland*

This is a pilot study in which all 52 cases of cancer of the paranasal sinuses recorded during 1970-1973 and their age-matched controls have been identified in the Finnish Cancer Registry. After confirming the diagnoses in the hospitals, questionnaires concerning the occupational histories will be sent to the patients or their relatives. The present study will be followed by an Inter-Scandinavian prospective case-control study.

214. INCIDENCE OF TESTICULAR TUMORS WITH EMPHASIS ON POSSIBLE RURAL PREPONDERANCE AND OCCUPATION

Sandeman, T. F., Matthews, J., Stone, J., Peter MacCallum Hospital, Urological Service, *278 William St., Melbourne, Victoria 3000, Australia*

Previous surveys of the testicular tumor population presenting to the Peter MacCallum Clinic have suggested an increased incidence of patients from rural areas. Articles published since then have confirmed this trend overseas. Futhermore, evidence in the literature indicates occupational risks for a large number of cancers. Two studies are being carried out: (1) A survey of all testicular neoplasms in the State of Victoria from 1950 to 1978, using records from pathology laboratories, to determine any increase in incidence and possible rural preponderance. (2) A case-control study of cases at Peter MacCallum since 1952, investigating residence (metropolitan, town or rural), occupation, place of birth, religion and possible exposure to carcinogens. All cases have been histologically classified to reveal relationships according to classification. Retrospective studies covering all the available case material are being carried out (a) to increase the numbers and (b) to detect any change in trends, and a survey of pathologists' records is being conducted.

215. CASE-CONTROL STUDY ON URINARY BLADDER CANCER

Puntoni, R., Valerio, F. O., Vercelli, M., Santi, L., Merlo, F., Universita degli Studi di Genova, Inst. de Oncologia, Dept. of Epidemiology, *Viale Benedetto 15, Pad. B, 16132 Genoa, Italy*

A random sample of 100 persons with urinary bladder cancer, all resident in the Genoa District, reported to the cancer registry is being compared with 200 persons of the same sex and age group affected by different diseases (excluding cancers and other diseases of the respiratory system, cancer of the upper alimentary tract, myocardial infarction, diseases of the urinary system and certain occupational diseases), admitted to the same hospital. Emphasis is placed on occupation and smoking habits. The objective of this study is to uncover possible associations between occupational exposure to chemical carcinogens and urinary bladder cancer.

216. ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN THE ETIOLOGY OF HUMAN BLADDER CANCER

Connolly, J., University of Toronto, *Medical Sciences Bldg., Toronto, Ontario*, M5S 1A8, Canada

To study the association between occupation, dietary and social patterns and bladder cancer, 348 bladder cancer patients (248 males, 100 females) and 2 controls per case (matched by sex, age within 5 years, and geographical location) were interviewed. Information was obtained about occupation (including contact with fourteen classifications of industrial chemicals), family background, past illnesses, analgesic intake, beverage consumption, smoking habits. The data are being analyzed.

217. BLADDER CANCER MORTALITY IN CERTAIN AREAS AND INDUSTRIES

Davies, J. M., Inst. of Cancer Research, Division of Epidemiology, *Clifton Ave., Sutton SM2 5PX, England, United Kingdom*

A number of towns have been selected, most of which are important centers for industries suspected of giving rise to a bladder cancer risk. As a first step male and female bladder cancer mortality rates in these towns over some 25 years will be compared with national and regional rates. As a second step a total of some 3,000 death certificates of male residents dying with bladder cancer ('cases') will be matched with 'control' death certificates of male residents dying from other causes at the same ages and dates; the occupations of cases and controls will be compared, using the occupations recorded on the death certificates.

218. CASE-CONTROL STUDY OF THE OCCUPATIONAL AETIOLOGY OF CANCER OF THE URINARY BLADDER

Tola, S. A., Korkala, M. L., Tenhu, M., Inst. of Occupational Health, Dept. of Epidemiology & Biometry, *Haartmaninkatu 1, SF00290 Helsinki 29, Finland*

Some 278 cases of cancer of the urinary bladder were reported to the Finnish Cancer Registry during 1975-1976. The diagnosis will be confirmed in the respective hospitals and age-matched controls will be selected from the patients of those hospitals. Questionnaires with special emphasis on occupational history will be sent to cases and controls. The analysis of the data will focus on comparison of occupational histories.

219. LUNG CANCER - HISTOLOGY AND OCCUPATIONAL EXPOSURE

Geddes, M., Buiatti, E., Falciani, C., Mugnaini, C., Nozzoli, F., Santucci, M., Seniori Costantini, A., Center for the Prevention of Social Diseases, Epidemiological Research in Environmental Toxicology Unit, *171 Viale Alessandro Volta, 50131 Florence, Italy*

An association has been observed between some occupations and specific histological types of lung cancer. The present study aims to verify if there is a different distribution of workers and others between various histological types of lung cancer, and to determine if there is a different distribution of occupational groups specifically exposed to carcinogens for lung in humans (IARC working group report, 1978) in lung cancer patients with different histological types and in controls. Approximately 500 lung cancer patients (males and females), with established histological diagnosis according to a simplified WHO classification, and an equal number of controls selected from the same hospital, without respiratory diseases, hospitalized in the same year, and matched for sex, age, residence and smoking habits are interviewed about occupational history, which is classified according to the International Labor Organization classification.

220. STUDY OF CANCER OF THE LUNG AND STOMACH, AND OF BRONCHITIS MORTALITY IN RELATION TO URBAN FACTORS

Waller, R. E., Medical Research Council, *20 Park Crescent, London W1N 4AL, England, United Kingdom*

This is a study based on published mortality data. One of the features of the distribution of lung cancer deaths in recent decades has been the relatively high rate in urban areas, but the pattern is changing gradually and the death rates currently experienced by recent cohorts are not much higher in urban than in rural areas, a change most marked in London. These findings are being considered in relation to the substantial

changes in pollution by smoke, as well as changes in smoking habits, and possible biases introduced by selective migration. The data have been accumulated gradually, as they become available, starting with deaths in 1951, and the object is to assess the trends over a 25 year period, arranged on a cohort basis. Data from this study for the Greater London area are also being used in connection with an investigation of lung cancer incidence among London Transport workers, over a similar 25 year period. The experience of the London Transport group as a whole is being compared with that of the general population, and incidence rates are being calculated for several job categories with a view to exploring the effects of exposure to diesel fumes.

221. OAT CELL CARCINOMA - INQUIRY INTO OCCUPATIONAL RISKS IN THE RHONE-ALPS AREA

Mouriquand, J. C., Centre National de la Recherche Scientifique, Cytology Lab., *B.P. 217X, c/o Centre Hospitalier, 38043 Grenoble, France*

OBJECTIVE: An evaluation of occupational risk of 293 cases of oat cell carcinomas is compared to a similar number of patients with squamous cell carcinomas of the lung.

APPROACH: The surgery rests upon 2581 cases of lung carcinomas diagnosed by cytology from January 1970 to July 1977, in the general population of the Rhone-Alps area. Patients have been classified according to their trades.

Preliminary results show that the occupational risk of oat cell carcinoma and squamous cell carcinoma is shared by some trades. Some other trades have an increased risk for oat cell carcinoma which deserves to be studied.

222. EPIDERMOID AND SMALL CELL CARCINOMAS OF THE LUNG - OCCUPATIONAL DISTRIBUTION AMONG THE WORKING POPULATION OF THE RHONE-ALPES AREA

Mouriquand, J., Paramelle, B., Ollagnier, R., Gally, A., Mayer, M., Jacouton, R., Bel, J., Patin, R., Morin, B., Bertherat, J., Universite de Grenoble, Faculte de Medecine, Laboratoire d'Histologie, *38700 La Tronche, Grenoble, France*

Epidermoid and small cell carcinomas are the main contributors to the recent increase in lung carcinomas, although the clinical course and the histological aspects of the two are quite different. Potential risk factors for lung cancer have been defined mainly within factories where the working population was submitted to defined substances (chrome, nickel, etc.), and few studies have examined the general working population. This retrospective study is based on 585 cases of epidermoid carcinoma and 200 cases of small cell carcinoma of the lung. Patients were classified according to their occupation and the age at occurrence of the disease. Occupational distribution and age groups were correlated with a cohort of non-cancer patients with lung diseases for whom cytological sputum specimens were sent to the laboratory, and with the professional distribution of the active population of the same area as obtained from the 1975 census.

223. EPIDEMIOLOGIC STUDIES ON MALE LUNG CANCER IN NORTHERN SWEDEN

Larsson, L. G., Sandstroem, A., Damberg, L., Johnsson, M., Regionsjukhuset, Dept. of Oncology, *90185 Umea, Sweden*

In a study of the geographical distribution of all new male lung cancer cases in the three northernmost counties in Sweden between 1959 and 1971 great differences were found between different regions. Some communities with mining districts or other heavy industry had age-adjusted incidence rates 10-15 times higher than more rural communities. The occupational profile of te cancer cases is being compared with that of a control series matched by age and place of residence. Information about occupation is obtained both for the cases and for the randomly selected controls through the general population register. For deceased male lung cancer cases registered in the same region from 1972 to 1977, a more detailed case-control study is being performed based on questionnaires to relatives about occupation, employment and smoking habits.

224. POPULATION-BASED CASE-CONTROL STUDY OF RESPIRATORY CANCER AND EMPLOYMENT HISTORY

Glazer, E. R., Dunn, J., Brand, R., Chiang, M., Hauck, M., State Dept. of Health Services, *1450 Broadway, Oakland, California*, 94612, United States of America

The objective of this study is to assess the effectiveness of a retrospective population-based study as a tool for the surveillance of occupational cancer. Detailed information on occupational and smoking histories and other relevant variables will be obtained for all respiratory cancer cases generated in one year by a geographically defined population of approximately one million. Past incidence trends indicate that this should amount to some six- to seven-hundred cases.

Questionnaires will be administered to cases as soon as possible after diagnosis. One control, matched for sex, race, ten-year age group and area of residence will be selected for each case.

225. PRIMARY LUNG CANCER INCIDENCE IN A HIGH RISK GROUP IN AN INDUSTRIAL POPULATION

Krzysko, R., Zielniewicz, B., Marciniak, J., Kaczmarek, A., Broniewska, J., Regional Lung Diseases Control Centre, Unit of Operational Research, *Szamarzewskiego 62, 60569 Poznan, Poland*

The study group of an estimated 40,000 persons has routine cytology and mass miniature radiography (MMR) every four months following collection of a personal medical history. These individuals will be followed for the next five years as well as a control group of some 50,000 persons with a routine yearly MMR examination. A pilot study involving 1,500 persons randomly selected from the study population and of 1,00 controls has now been completed.

226. ENVIRONMENTAL EXPOSURES AND CHILDHOOD LEUKEMIA

Pendergrass, T. W., Children's Orthopedic Hospital & Medical Center, Division of Hematology & Oncology, *4800 Sand Point Way N.E., Box C-5371, Seattle, Washington*, 98105, United States of America

Little is known of the role of parental occupational exposures or perinatal drug ingestion in the subsequent development of childhood acute lymphocytic leukemia. This study has two goals: a) development of a method for obtaining information on parental occupational and perinatal drug exposures, and b) testing of this method on parents of children diagnosed as having acute lymphocytic leukemia, between 1972 and 1979, in the State of Washington. Cases have been identified in the three major hospitals treating children with cancer in the State. For each case a hospital control has been selected to attempt to control for any differences in recall between parents of ill and presumably well children. General population controls will be obtained by use of a random digit dialing method. To date, 80% of case parents have been interviewed. Occupational data include a detailed review of occupational history and review of each job-related exposure. A detailed review of perinatal drug ingestion is obtained.

227. ASSOCIATION OF PARENTAL OCCUPATION WITH CHILDHOOD CANCER CASES - NCI

Spirtas, R., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Current studies of the association between industrial agents and reproductive effects have focused on health outcomes prior to and including delivery. For those pregnancies resulting in 'normal' live births, it is possible that later (after one year) adverse effects such as neoplasms could be directly associated with exposures from agents identified in the occupational/industrial groups of the mother and/or father of a child.

The purpose of this proposed project is to survey childhood cancer cases in an attempt to provide an overview of associations between certain malignant neoplasms and parental occupational/industrial groups and to suggest studies of specific occupational/industrial groups that indicate excess cancer risk for workers' offspring.

The work on the project would be carried out under contract. The contractor would abstract, code, and analyze a

data set of childhood cancer cases to accomplish the define purposes of the project.

FY 79 ACCOMPLISHMENTS: An interagency agreement between the Food and Drug Administration and NIOSH was completed.

228. CHILDHOOD CANCER AND PARENTS' OCCUPATION

Hemminki, K. J., Partanen, T. J., Salonen, T., Inst. of Occupational Health, Dept. of Industrial Hygiene & Toxicology, *Haartmaninkatu 1, SF00290 Helsinki 29, Finland*

The study aims to find out whether any correlation exists between the occupational activities of parents and cancer in their children. The material consists of cancer cases in children under 15 years of age recorded by the Finnish Cancer Registry in the period 1959-1968. The parents' occupations were traced from the records of the antenatal clinics. Controls were matched for age and place of birth. The material is being analysed with regard to the occupation of the parents.

229. FIELD STUDIES IN HIGH-RISK AREAS

Blot, W. J., Fraumeni, J. F., Hoover, R., Mason, T. J., Stone, B. J., Pickle, L., Brinton, L., Mendelsohn, L., Morris, L., Lubin, J., Tagnon, I., Ziegler, R., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst., Analytical Studies Section, *9000 Rockville Pike, Bethesda, Maryland,* 20205, United States of America

The objectives of this project are to identify and describe environmental and host determinants of cancer in areas of the U.S. at high risk of cancer through the use of analytical epidemiologic techniques, particularly case-control studies of specific cancers. Completed during the year were interview studies of (a) respiratory tumors in Tidewater, Virginia, which showed a 70% smoking-adjusted excess of lung cancer and a 1500% increase of mesothelioma associated with employment, primarily during World War II, in area shipyards; (b) esophageal cancer among black males in Washington, D.C., which revealed a dominating effect of alcohol consumption, although other interesting nutritional differences were also uncovered; and (c) colorectal cancer in rural Nebraska which identified an increased risk among persons of Czechoslovakian descent and a familial clustering. Also completed was a death certificate review of lung and pancreatic cancer in Louisiana; results indicated an excess of petroleum industry occupations associated with both of the cancers and shipbuilding employment associated with lung cancer and a higher frequency of lung cancer among the older Acadian (Cajun) minority.

BIBLIOGRAPHIC REFERENCES: Blot, W.J. and Fraumeni, J.F., Jr.: Lung cancer in the United States: Shipyard correlations. Ann. N.Y. Acad. Sci. 330: 313-316, 1979. Pickle, L.W. and Gottlieb, M.S.: Pancreatic cancer mortality in Louisiana. Am. J. Public Health. 70: 256-259, 1980.

230. LONG-TERM EFFECTS OF THE HEALTH STATE OF OCCUPATIONAL EXPOSURES TO CHEMICALS

Maties, R., Muica, N., Ghise, O., Tanase, T., Modorcea, V., Sabau, P., Horvath, P., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Medicine, *Strada Biserica Amzei 29, Bucharest, Romania*

Malignant tumors as well as cardiovascular and obstructive lung diseases may be caused by occupational exposure to various chemicals. The aims of the project are (1) to develop a suitable epidemiological methodology; (2) to analyze accurately the long-term effects of occupational exposure to chemicals, and (3) to determine the specific patterns of morbidity and mortality from malignant tumors in workers formerly exposed to chromium salts, asbestos and aromatic amines. The project includes a study of mortality from lung cancer, pleural mesothelioma and bladder cancer over the last 20 years in workers exposed to various chemicals, compared to the mortality recorded in the general population of the area, and a morbidity study based on the result of periodic medical examinations performed annually among workers at risk.

231. STUDY OF OCCUPATIONAL CANCERS

Horbach, L., Duhme, C. F., Guggenmoos, I., Loskant, L., Friedrich Alexander Universitat zu Erlangen Nurenberg, Institut fuer Medizinische Statistik und Dokumentation, *Waldstr. 6, D8520 Erlangen, Federal Republic of Germany*

The aims of this study are: (1) to survey manual workers and other staff employed in chemical and related industries for cancer and (2) to analyze possible aetiological associations between different cancer sites and occupational chemical exposures. In this retrospective study of the years 1950-1968 all ill and/or deceased employees (active or retired) of 10 large firms have been included and for the same time period all other deaths from one of those firms also have been collected. Information has been collected on sex, cause of death, occupation, substance to which exposed and for the cases of cancer: type of neoplasm, age at time of diagnosis and method of diagnosis. For the statistical analysis a multivariate model is being used. In February 1979 a detailed description of the study (more than 400 pages) was presented; it should be discussed in several expert groups in April and in autumn 1979. The study will be published in 1980 in a research report of the DFG.

232. OCCUPATIONAL CANCER RISK ESTIMATION IN CHEMICAL INDUSTRY

Barhad, B., Maties, B., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Medicine, *Strada Biserica Amzei 29, Bucharest, Romania*

A survey to establish the number of workers exposed to carcinogenic chemicals has been carried out in several large plants in the chemical industry. The data have been correlated with levels and lengths of exposure and cancer morbidity. The study aims to develop better methods of circulating information about workers exposed to carcinogenic substances, taking into account movement of the worker population, retirement and the expansion of the chemical industry, and to apply primary and secondary preventive measures to exposed individuals.

233. OCCUPATIONAL DISEASE IN ALBERTA WORKERS EXPOSED TO CHEMICALS

Fincham, S. M., Hill, G. B., Hanson, J., Dewar, R., Alberta Provincial Cancer Hospitals Board, Dept. of Epidemiology, *11560 University Ave., Edmonton, Alberta,* T6G 1Z2, Canada

A data base was established on a cohort of 5,777 Alberta workers occupationally exposed to chemicals and 1,645 workers not so exposed. The data file will be matched annually with the Alberta Cancer Registry and the National Death Registry using record-linkage techniques. Risk estimates will be computed for cancer incidence and for cause-specific death in both groups.

234. CANCER INCIDENCE AMONG EMPLOYEES IN THE CHEMICAL INDUSTRY

Ahlbom, A. O., Norell, S. E., Olin, R. G., Huddinge Sjukhus, *S14186 Huddinge, Sweden*

The aim of the study is to assess the association between chemical exposure at work and leukemia and brain tumors. The study is based on the Swedish Cancer Registry. This was linked to the census of 1960 which included information about occupation. The material consists of cases reported to the Registry during the period 1961 to 1973.

235. ANALYSIS OF CANCER RISK DISTRIBUTION FOR CHEMICALS IN THE WORK ENVIRONMENT

Puntoni, R., Vercelli, M., Merlo, F., Buiatti, E., Geddes, A., Santi, L., Istituto di Oncologia, Dept. of Epidemiology, *Viale Benedetto XV, Pad. B, 16132 Genoa, Italy*

A census of all the industries (including tradesmen) in the industralized town of La Spezia, with 130,000 inhabitants, is being organized in order to study the distribution (use, quantity, number of exposed) of compounds selected from the list of carcinogens published by IARC (Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man). The objective is to quantify the presence of chemical carcinogens in the environment and to formulate hypotheses about the effects of such compounds on the health of the exposed people. This study is undertaken in collaboration with 'Centro per le malattie sociale' of Florence.

236. STUDIES OF OCCUPATIONAL CANCER

Blair, A. E., Blattner, W., Grauman, D. J., Mason, T. J., Miller, B., Greene, M., Mendelsohn, L., Cantor, K., Dalager, N., Lubin, J., Stone, B. J., Spirtas, R., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst., Occupational Studies Section, *9000 Rockville Pike, Bethesda, Maryland,* 20205, United States of America

This project involves identification of cancer patterns among occupational groups that may reflect exposures in the work environment and investigation of methodological issues in occupational studies. Study groups are selected because of 1) known or potential exposure to established or suspect carcinogens, 2) prior reports suggesting an unusual cancer experience for the group, 3) requests by outside institutions, and 4) availability of useful resources. Resources used included employment and death records maintained by companies, labor unions or professional organizations, and records from government agencies. Studies during the past year include cohort mortality studies of persons employed in dry cleaning, non-agricultural pest control, chemical plants, non-ferrous smelters, taconite mines, jewelry manufacturing, embalming, welding, shipyards, chemical and medical laboratories, ship inspection, and hematite mining. Proportionate mortality studies being conducted involve tobacco workers, petrochemical workers, pottery workers, fur dyers, veterinarians, and embalmers. Death certificates are used to investigate occupational origins of leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, and cancers of the prostate and colon.

BIBLIOGRAPHIC REFERENCES: Blair, A.: Mortality among workers in the metal polishing and plating industry, 1951-1969. J. Occup. Med. 22: 158-162, 1980. Blair, A. and Hayes, H.M.: Cancer and other causes of death among U.S. veterinarians, 1966-1977. Int. J. Cancer. 25: 181-185, 1980.

237. CASE-CONTROL STUDY OF CERTAIN CANCERS AND EXPOSURE TO VARIOUS INDUSTRIAL ACTIVITIES IN A TOWN

Sjoeberg, A., Axelson, O., Boliden Aktiebolag, Chemicals Division, *25100 Helsingborg, Sweden*

Many malignant diseases have a far higher urban than rural incidence. Possible associations between the incidence of certain cancers and exposure to various industrial activities will be investigated and the proportion of morbidity attributable to such industrial sources elucidated. All cancer cases recorded for the town of Helsingborg (population about 80,000) in the Swedish National Cancer Register for the years 1958 to 1971 will be used for a case-control study. Two controls will be sought for each case with respect to sex, age and place of abode. Exposure is defined as previous occupation in some factory or factories or other defined activity. Employment rolls from, for example, inorganic chemical works, a rubber factory, a pharmaceutical laboratory, a shipyard or the local hospital will be studied. The exposure criteria will be as specific as possible. Resident industrial medical officers will cooperate in the project.

238. CANCER SURVEILLANCE OF OCCUPATIONAL COHORTS IN A WESTERN SMSA - NCI

Sestito, J., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

This project proposes the examination of cancer incidence patterns among selected occupational cohorts in the greater San Francisco-Oakland SMSA. Numerous unions and collective bargaining organizations maintain data on constituent members. Given existing data on known and suspected carcinogenic hazards present in the environment of these cohorts, the existence and applicability of union data facilitates the study of the occupational cohorts for unusual cancer incidence. Linkage of data such as this with data on cancer incidence in geopolitically defined populations provides direct comparison of cancer risks for selected occupational groups. The results of such efforts will assist industry-wide studies in identifying groups at risk and thus encourage a finer characterization of the occupational environment. These activities will benefit NIOSH programs in criteria document development and OSHA's program of standard setting. This particular project also explores the methodologic and technical problems associated with population-based cancer surveillance. The nature of the study necessitates a cooperative effort between the SEER participant in the Bay Area and NIOSH. A contract will be developed for basic data collection, update, edit, and preliminary analysis.

FY-79 accomplishments: Seven unions, representing 16 union locals or approximately 9400 individuals, have been identified for study. Data files are being constructed to facilitate cancer registry linkage and cancer incidence determination.

239. EPIDEMIOLOGICAL STUDY OF THE INCIDENCE OF CANCER AS RELATED TO INDUSTRIAL EMISSIONS IN CONTRA COSTA COUNTY

Austin, D. F., Riggan, W. B., State Dept. of Health Sciences, California Tumor Registry, *2151 Berkeley Way, Berkeley, California*, 94704, United States of America

The study aims (1) to test the hypothesis that the incidence of cancer of specific sites is higher in the population of the heavily industrialized section of Contra Costa County than in the population of the residential areas; (2) to determine whether any union or occupational groups in Contra Costa County have higher incidence rates for any cancer sites than other unions or occupational groups; (3) and to identify specific environmental factors associated with lung cancer incidence in Contra Costa County. Age, race, sex and site specific cancer incidence rates for an 8 year period will be calculated for the group of census tracts in the predominantly industrial section of Contra Costa County and for the remaining group of tracts in the residential section. Rosters of union members and other occupational groups will be matched with cancer incidence files of the Resource for Cancer Epidemiology. The number of cases observed will be compared in the San Francisco-Oakland SMSA. A case-control study of cancer patients in Contra Costa County will be performed. The site, sex and age of the cancer patients will be decided on the basis of the results of the cancer incidence data obtained in the first part of the study. A questionnaire designed to investigate variables, such as length of residence in Contra Costa County, socioeconomic status, smoking, occupation and other causative and contributing variables, will be administered to cases and controls.

240. CASE-CONTROL STUDY USING SSA IDENTIFICATIONS

Halperin, W., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

This study presents a new methodologic approach to linking disease in a geographic area to an occupational etiology. Examples include bladder cancer in New Jersey and leukemia or brain tumors in east Texas. The Social Security Administration records the employer, for each contributor, for each quarter. For any individual, reconstruction of a continuous employer history is feasible.

We propose first to ascertain cases of a particular disease, such as bladder cancer in New Jersey, and controls, consisting of New Jersey citizens of similar age, race, and sex with other causes of death. SSA would then provide continuous work histories for cases and controls. Specific employers or categories of employers represented in excess among cases as compared to controls may then be identified. These industries or employers would then be subject to in-depth cohort mortality studies. The cohort mortality study may identify new etiologies for the disease in question or identify continuing exposures to known carcinogens.

241. EPIDEMIOLOGICAL STUDY ON THE HOST-ENVIRONMENT INTERACTION IN HUMAN CARCINOGENESIS

Fukuma, S., Shimamura, K., Murata, M., Tanaka, N., Chiba Cancer Center Research Inst., Division of Epidemiology, *666-2, Nitona-Cho, Chiba 280, Chiba, Japan*

OBJECTIVE: It is generally accepted that human cancers are mainly caused by the carcinogenic effect of environmental materials, e.g., tobacco and food additives. Some occupations may also be included among such environmental factors, but they have not yet been adequately studied in many countries. Furthermore, it is also hypothesized that hereditary factors for cancer liability interact with environmental ones and intensify their hazardous effect, but at present there are few demonstrable examples of the host-environment interaction in epidemiological studies. The object of our study is, first, to identify any occupations with suspected high risk of cancer and, second, to examine whether any synergistic effects of familial cancer history and occupational factors can be found.

APPROACH: Data are available in the hospital records of Chiba Cancer Center Hospital and the population-based Cancer Registration Center of Chiba prefecture.

PROGRESS: Data accumulation and analysis are ongoing.

242. PROPORTIONAL OCCUPATIONAL ANALYSIS USING DEATH CERTIFICATE DATA

Marrett, L. D., Meigs, J. W., Connecticut Cancer Epidemiology Unit, Dept. of Epidemiology & Public Health, *30 College St., New Haven, Connecticut,* 06510, United States of America

Occupational data for a random sample of 8,000 Connecticut adults who died between 1959 and 1961 have been collected and coded. Occupation, industry, birthplace and cause of death for this general population sample will be compared with those of deceased Connecticut Tumor Registry incidence cancer cases. Such analyses will control for sex, age at death, and socioeconomic status. These data are currently being used in the studies of occupational factors in urinary bladder cancer and chronic leukaemia in Connecticut. It is hoped that the results of these and similar studies on other cancer sites will suggest new hypotheses regarding associations between occupational exposures and subsequent cancer experience.

243. EVALUATION OF OCCUPATION AS RECORDED ON DEATH CERTIFICATES

Wigle, D. T., Lindsay, J., Howe, G. R., Mao, Y., Canadian Dept. of National Health & Welfare, Lab. Centre for Disease Control, *Tunneys Pasture, Ottawa, Ontario,* K1A 0L2, Canada

The death certificates for about 3,000 persons dying of cancer and previously included in random samples of the Canadian Labor Force have been examined to retrieve recorded information concerning major lifetime occupations. The occupations have been coded using standard occupational coding manuals prepared for use in the decennial census. The coded occupations will be compared with those previously recorded when the individuals were interviewed during the Labor Force Survey.

244. CANCER AND THE INDUSTRIAL ENVIRONMENT

Lloyd, O. L., Ogston, S., Mair, A., University of Dundee, Ninewells Medical School, Dept. of Community & Occupational Medicine, *Dundee DD1 9SY, Scotland, United Kingdom*

Environmental influences, many of them industrial, have been held to be responsible for the vast majority of human cancers. This study aims to analyze the patterns of mortality within relatively small populations in Scotland to identify areas where the incidence (or mortality) of specified cancers is abnormally high. It is intended to investigate the environment of these areas in order to try and identify possible carcinogenic factors. It is hoped that the occupational experience of the deceased can be evaluated in order to determine whether or not carcinogenic factors were in the occupational environment or in the more general environment. Evaluation of the environment will be assisted by the collaboration of the Scottish Occupational and Environmental Health Service, Ninewells Medical School, Dundee.

245. CANCER AND OCCUPATIONAL EXPOSURE TO INDUSTRIAL POLLUTANTS

Kjuus, H., Langard, S., Lien, J. T., Lislerud, A., Lyngdal, P. T., Moen, H., Omland, H., Telemark Sentralsjukehus, Dept. of Occupational Medicine, *Olavsgt. 26, 3900 Porsgrunn, Norway*

Suggested estimates of the proportion of cancers attributable to occupational exposure varies widely. This case-referent study aims to assess to what degree cancer among patients in a county hospital is related to occupational exposure. A complete working history is obtained from all male patients admitted to surgical and medical wards with newly diagnosed cancer, and the total number of years of occupational exposure to a variety of industrial pollutants is recorded. The reference group consists of age-matched non-cancer patients from the same wards. There will be approximately 100-150 cancer patients in the case group.

246. RELATION BETWEEN CANCER INCIDENCE AND ENVIRONMENTAL FACTORS

Rylander, C. R., Axelsson, G., Goteborgs Universitet, Dept. of Environmental Hygiene, *411 Vasaparken, S40010 Goteborg, Sweden*

The geographical distribution of various types of neoplasms is studied in Sweden. Register data on liver cancer in males indicate that the three big cities in Sweden have an increased rate in comparison to the remainder of the country and that the rate has increased the last 10 years. This difference is less pronounced among females. Further analyses using hospital records are performed to investigate the possible causes of this difference, with particular reference to occupational exposure and alcohol consumption.

247. OCCUPATIONALLY RELATED CANCER

Howe, G. R., Miller, A. B., University of Toronto, *Medical Sciences Bldg., Toronto, Ontario,* M5S 1A8, Canada

Employment records for a 10% sample of the Canadian Labour Force from 1965 to 1968, and for a (different) 5% sample for 1969 to 1971 (a total of about 600,000 individuals) are being linked, using computer techniques, to the national mortality and cancer incidence data bases maintained by Statistics Canada. The objective is to determine mortality from all causes and cancer morbidity for the various occupations and industries represented in the cohort.

248. CANCER MORTALITY RELATED TO OCCUPATION AND SOCIAL CLASS

Esteve, J., World Health Org., *150 Cours Albert Thomas, Lyon, France*

OBJECTIVE: Work on the obtainment, examination, review, and interpretation of data relating to cancer mortality that have been produced historically in successive studies from the General Registrar Office of England and Wales. This shall include analysis of the relationship of mortality from cancer to occupation and social class, analysis of trends over time, as well as comparison with relevant material from other countries. This analysis shall be performed in collaboration with the Project Officer.

249. CANCER MORBIDITY IN NEW ZEALAND IN RELATION TO OCCUPATION

Kjellstrom, T., Foster, F. H., University of Auckland, Dept. of Community Health, *P.O. Box 2175, Auckland, New Zealand*

The study, which will be based on new cases registered at the New Zealand National Cancer Registry during 1972-74, will describe differences in cancer morbidity between occupational groups of adult males in New Zealand. The findings will be examined in relation to earlier studies and to possible differences in the working environment of the occupational groups.

250. OCCUPATIONAL CANCER RISK IN HAWAII

Mi, M., University of Hawaii System, Manoa Campus, John A. Burns School of Medicine, Dept. of Genetics, *2444 Dole St., Pacific Biomedical Res. Ctr., Honolulu, Hawaii,* 96822, United States of America

Provide data which will permit the linkage of official records: Civil Defense file, birth records, and death certificates for the population of Hawaii from 1942 to the latest year available with specific emphasis on occupation and/or place of employment.

251. EPIDEMIOLOGICAL STUDY ON CANCER PATIENTS

Hirohata, T., Kurume University, Dept. of Public Health, *67 Asahi-Machi, Kurume City 830, Fukuoka, Japan*

In cooperation with a large hospital in Kyushu, pilot case-control studies examining exposure to unusual chemicals and employment in unusual occupations are being conducted.

III. POLLUTION AND OTHER ENVIRONMENTAL FACTORS ASSOCIATED WITH HUMAN CANCER

A. AIRBORNE ENVIRONMENTAL POLLUTION

252. HEALTH EFFECTS IN CHILDREN EXPOSED TO VINYL CHLORIDE

Ziskind, R. A., Wilkinson, G. S., Science Applications Inc., Energy Environment Systems Division, *1801 Ave. of the Stars,*

Suite 1205, Los Angeles, California, 90067, United States of America

Although a considerable body of occupational and laboratory toxicological data have demonstrated the carcinogenic action of vinyl chloride monomer (VCM), there appears to be little epidemiological information regarding health effects in children exposed to ambient levels of VCM. A pilot study consisting of a cohort of elementary school children who attended a school situated in close proximity to a PVC manufacturing plant will be conducted for potential health effects 10 to 20 years after exposure. Students will be grouped into three graduated exposure categories based upon estimates of total VCM concentrations received. Plant production history will be linked with pupil records, air monitoring data and dispersion calculations to subgroup the cohort. A number of mortality and morbidity indicators and data bases will be examined in order to contrast all exposure groups with zero exposure population.

253. CORRELATION OF AIR POLLUTION AND CANCER

Oomen, J. M., Muir, C. S., Hoedenmaker, F., Van der Esch, E. P., Schneider, T., Van der Heyden, C. A., Kreis, I. A., National Inst. of Public Health, Div. of Epidemiology & Regional Lab., *P.O. Box 1, 3720BA Bilthoven, Netherlands*

In this collaborative project between the International Agency for Research on Cancer and the National Institute for Public Health (RIV) a correlation study between air pollution and cancer will be developed, which will exploit the unique automated system of air pollution monitoring existing in the Netherlands. The pollution data collected are such that it is possible to produce an integrated average exposure to sulphur dioxide, the oxides of nitrogen, ozone and carbon monoxide, for a large number of areas covering the entire country. The Netherlands National Vital Statistics Office will be consulted for information on cancer and other death rates, for the areas considered to be meaningful for atmospheric pollution exposures. The Automated Pathological Diagnoses Storage and Retrieval System (PALGA) has an important potential for epidemiological studies as the information about cases of cancer is based on histological diagnoses.

254. RELATIONSHIP BETWEEN AIR POLLUTION AND CANCER IN JAPAN

Tominaga, S., Kuroishi, T., Shimizu, H., Ogawa, H., Nakagawa, N., Hirose, K., Aichi Cancer Center Research Inst., Division of Epidemiology, *81 1159 Kanokoden Tashiro-cho, Chikusa-ku, Nagoya 464, Aichi, Japan*

This study aims to clarify the relationship between air pollution and cancer mortality. Sulphur dioxide (SO2) and nitrogen oxide (SO2) levels and dustfall were used as indexes of air pollution. The average value of each pollutant for each of the 46 perfectures (1967-1975) was related to the age-adjusted mortality rates of cancers of the lung, esophagus, stomach, breast and uterus (1975) for the corresponding prefecture. In examining relationships between air pollution and cancer mortality, smoking was also taken into account. The relationship between SO2 and lung cancer and breast in females and those between NO2 and lung cancer in both sexes and breast cancer in females was statistically significant after taking into account the proportion of smokers. Analysis continues.

255. RISK OF NEOPLASIA IN NEIGHBORHOOD ASBESTOS DISEASE

Hammond, E. C., Selikoff, I. J., Garfinkel, L., American Cancer Society Inc., Dept. of Epidemiology & Statistics, *777 3rd Ave., New York, New York,* 10017, United States of America

It is known that mesothelioma can occur in relatives of asbestos workers. However, it is not known whether or not mesothelioma or lung cancer occurs with greater frequency in persons with low-level exposure, for example, those living near an asbestos plant. We have established a cohort of all males over the age of 18 living within a half mile of an asbestos plant in Paterson, New Jersey, 1942-1943; there were approximately 2,500 such individuals. As a control group, we have listed a cohort of men with identical qualifications in another neighborhood of the same city, with similar social strata, but without an asbestos facility. All members of both cohorts are being traced through 1974 and their mortality experience evaluated. We have successfully traced over 95 percent of both groups. In addition, lung tissue of those who have died is being analyzed for its asbestos content, quantitatively, and settled dust in homes at varying distances from the index factory, taken from attic rafters, etc., is being studied for its asbestos fiber burden. In both the epidemiological and environmental investigations, workers employed in the factory and their families are excluded. The first mortality analyses of these data are now completed. Total mortality, total cancer and lung cancer deaths did not differ in the two neighborhoods 20-35 years after first exposure. Follow-up will continue.

256. NORTH-EAST FLORIDA LUNG CANCER STUDY

Davies, J. E., Fraumeni, J. F., Blot, W. B., Nordwall, C., Duncan, R. C., Ng, A., Aldrich, T. E., University of Miami, School of Medicine, Dept. of Epidemiology & Public Health, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida,* 33152, United States of America

This study proposes to gather retrospective data concerning asbestos exposure on all new lung cancer cases in four north-east Florida counties. The study will consider occupational histories as well as smoking. The study will also locate geographically all cases and two matched controls to ascertain any possible clustering patterns associated with major air pollution sources in the area. Case verification has been performed by an independent pathology review and analysis is anticipated concerning morphological types of lung cancer and specific risk factors. The study is also identifying mesothelioma and asbestosis cases for the same time period (1978-79) and geographical area.

257. CANCER IN ARSENIC-EXPOSED POPULATIONS

Enterline, P. E., University of Pittsburgh, Graduate School of Public Health, Dept. of Biostatistics, *4200 5th Ave., Pittsburgh, Pennsylvania,* 15260, United States of America

The summary for this project is under entry no. 94.

258. CANCER INCIDENCE IN RELATION TO A SMELTER

Polissar, L., Fred Hutchinson Cancer Research Center, Epidemiology & Biostatistics Program, *1124 Columbia St., Seattle, Washington,* 98104, United States of America

The population in parts of King, Pierce, and Kitsap Counties of Washington State, U.S.A., are exposed to air-borne and soil-deposited arsenic trioxide from a smelter in Tacoma. Arsenic exposure has been linked to respiratory cancer among the Tacoma smelter employees and has been implicated as a carcinogen in other industrial studies. The effect of arsenic on cancer risk in the exposed populations outside the smelter will be evaluated using data from a complete, areawide cancer registry.

259. LUNG CANCER MORTALITY IN A POPULATION EXPOSED TO CHROMIUM DUST POLLUTION

Axelsson, G., Rylander, C. R., Goteborgs Universitet, Dept. of Environmental Hygiene, *411 Vasaparken, S40010 Goteborg, Sweden*

The population in a community in Sweden is exposed to air pollution which, to a significant degree, originates from a ferro-chromium industry. The total amount of chromium in the air is 50-200 times higher than background values elsewhere. Death rates in 1961-1975 in the exposed parishes will be compared to those in areas of the same size without chromium emission.

260. LUNG CANCER MORTALITY AND AUTOMOBILE EMISSIONS

Shimizu, H., Tominaga, S., Kuroishi, T., Aoki, K., Aichi Cancer Center Research Inst., Division of Epidemiology, *81 1159 Kanokoden Tashiro-cho, Chikusa-ku, Nagoya 464, Aichi, Japan*

To examine the causal association between exposure to vehicular emissions and lung cancer, the mortality rates for lung cancer (1969-1974) were analyzed among inhabitants living in the areas within 100 meters from main streets on which more than 1,000 cars pass daily from 7 am to 7 pm in Nagoya city. Traffic volume was regarded as an indicator of the degree of exposure to exhaust gas. The preliminary results show an increase in the standardized mortality ratio (SMR) of lung cancer in parallel with the traffic volume for males. However, for females the SMR was highest in the intermediate areas and did not parallel the traffic volume. No apparent relationships were observed between proximity to streets and lung cancer mortal-

ity. Mortality adjusted by smoking history, history of hazardous exposure and residential history showed similar results. The relationship between lung cancer mortality and traffic volume will be analyzed according to the histological type of lung cancer.

261. HEALTH EFFECTS IN THE PETROLEUM INDUSTRY

Alpen, E. L., University of California, Berkeley Campus, Lawrence Berkeley Lab., *Berkeley, California*, 94720, United States of America

The summary for this project is under entry no. 172.

262. CANCER MORBIDITY AND MORTALITY IN A ZONE OF CENTRIFUGAL SPREAD NEAR PESTICIDE FORMULATING PLANTS

Savage, E. P., Taylor, D. K., Colorado State University, Inst. of Rural Environmental Health, Epidemiologic Pesticide Study Center, *Spruce Hall, Fort Collins, Colorado*, 80523, United States of America

In recent years, the association between exposure to pesticides and the resulting health effects has been investigated. Much of this research has focused on the potential carcinogenicity of the chlorinated hydrocarbons. The effects of contamination of the areas surrounding pesticide formulating plants will be investigated in this study. It is reasonable to assume that the adjacent area, and also the area affected by the meteorological dispersion of contaminants, will experience a higher level of pesticide exposure than those areas outside this zone. The study population will consist of individuals living within specified areas of centrifugal spread in the proximity of three pesticide formulating plants in Colorado. The cancer mortality rate for these areas will be compared to that of a similar control population. Cancer mortality data will be collected from death certificate listings for the years 1970 to 1975. Households within the study population will also be interviewed to obtain morbidity data.

263. CANCER IN ILLINOIS

Epstein, S. S., Swartz, J., Melius, J., University of Illinois, Medical Center at Chicago, School of Public Health, Dept. of Occupational & Environmental Medicine, *Box 4348, Chicago, Illinois*, 60680, United States of America

The aim of this project is to investigate the contribution to cancer mortality of specific industrial manufacturing and processing activities in Illinois. Maps depicting mortality rates by county for Illinois on the basis of 1970-1976 data will be constructed. Major sources of carcinogens will be identified. Emissions data, ambient sampling, and dispersion models will be used to estimate levels of ambient exposures to carcinogens at different sites near the sources. Death certificates will be analyzed in order to compute mortality rates for cancer of several sites in tracts near the carcinogen sources. The tracts will be selected to control for confounding variables as much as possible. The relationship between cancer mortality rate, tract, and ambient exposure will be investigated. Possible carcinogen sources include: oil refineries, steel mills, metal refineries, chemical plants, and areas of high use of agricultural chemicals.

264. TEESSIDE STUDY

Dean, G., Wicken, A. J., Lee, P. N., Medico-Social Research Board, *73 Lower Baggot St., Dublin 2, Ireland*

The objectives of this study were to determine how, during a recent period, mortality from lung cancer, bronchitis, heart disease, and stroke related to air pollution, social class, smoking (with particular emphasis on whether the cigarette smoked was filter or plain) and other factors, and to examine changes in lung cancer and bronchitis mortality during the last ten years in relation to changes in air pollution levels and smoking habits. The surviving relatives of those people in Cleveland County who had died from lung cancer or bronchitis in 1969-72 (males) or 1969-1972 (females), heart attack in 1971-1972 (males only) or stroke in 1966-1972 (also males only) were interviewed. Details of a number of factors, including, in particular, the decedent's probable exposure to air pollution and smoking habits, were obtained. Similar information for the living population was obtained for a random sample in 1973. It was thus possible to relate mortality to the factors measured and also to compare mortality rates from lung cancer and bronchitis with those of the similar study carried out in Teesside in 1963. The study is to be published in two parts by the Tobacco Research Council, London, as their Research Paper 14 'Report on a second retrospective mortality study in North-East England'. Part I 'Factors related to mortality from lung cancer, bronchitis, heart diseases and stroke in Cleveland County, with particular emphasis on the relative risks associated with smoking filter and plain cigarettes' appeared in September 1977. Part II 'Changes in lung cancer and bronchitis mortality and in other relevant factors occurring in areas of North-East England 1963-72' appeared in the 1978 TRC Research Papers, 14.

265. LONG-TERM TRENDS IN STOMACH CANCER MORTALITY AMONG KRAKOW REGION INHABITANTS

Jedrychowski, W., Cholewka Cabaj, K., Popiela, T., Akademia Medyczna w Krakowie, Inst. of Social Medicine, Dept. of Epidemiology, *Ul. Kopernika 7, 31034 Cracow, Poland*

The aim of the study is to compare mortality from malignant gastrointestinal neoplasms in groups of inhabitants living in four city districts differing in their demographic features and nutritional habits. The analysis is based on death certificates and interviews regarding dietary habits carried out in representative samples of the inhabitants. The results of a preliminary study based on a 1974 survey show higher mortality rates for all causes, and for gastrointestinal neoplasms in particular, in the center of the city, with the exception of mortality due the stomach cancer in women, than among the suburban population. Mortality rates due to gastrointestinal neoplasms of the stomach, liver, gallbladder and pancreas, colon and rectum were also high in men living in the newly developed part of the city. The differences in the consumption patterns of basic food products failed to explain fully the observed divergence between the mortality rates. However, the higher mortality rates in the center of the city could be explained to some extent by the higher atmospheric pollution level.

266. CAUSES OF DEATH IN THE DIFFERENT QUARTERS OF GENOA

Puntoni, R., Valerio, F., Vercelli, M., Santi, L. I., Merlo, F., Universita degli Studi di Genova, Inst. de Oncologia, Dept. of Epidemiology, *Viale Benedetto 15, Pad. B, 16132 Genoa, Italy*

The city of Genoa (816,872 inhabitants) is subdivided into 25 quarters. The socioeconomic and environmental situation of these quarters is very heterogeneous and there are different levels of air pollution. The 20,000 deaths which occurred in the years 1970-71 are being analyzed by the quarter of residence the cause of death and the last occupation. The purpose of this investigation is to define possible relations between environment (different levels of air pollution), occupation and cause of death, with particular reference to cancer of the respiratory tract.

267. EPIDEMIOLOGICAL INVESTIGATION OF AN OUTBREAK OF MESOTHELIOMA IN CENTRAL ANATOLIA, TURKEY

Baris, Y. I., Simonato, L., Saracci, R., Hacettepe Universitesi, Faculty of Medicine, Dept. of Chest Diseases, *Ankara, Turkey*

The study consists of an epidemiological survey of selected villages (mortality by cause, main demographic features, examination of all adults with chest X-ray, questionnaire and medical examination) and environmental measurements of airborne dust with count size determination of fibers. The field investigation started in 1978 with two villages, one where an extremely high incidence of pleural mesothelioma had previously been documented and the other a nearby control village with no cases yet reported.

268. PILOT STUDY OF AMBIENT AIR POLLUTION AND SURVIVAL OF CANCER

Wilkinson, G. S., Priore, R., Reese, P., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., Population Studies Div., *Research Triangle Park, North Carolina*, 27709, United States of America

This study is concerned with analyzing potential relationships between reported levels of air pollution in the ambient air and length of survival for diagnosed cancer patients. Categorical indicators of pollution levels will be derived from data available from the National Aerometric Data Bank. Survival times for patients having histologically confirmed cases of cancer who have been accessioned into the Lakes Area Regional Tumor

Registry will be analyzed by life table and other appropriate methods. This investigation will permit preliminary statements about the effect that various concentrations of ambient air pollutants may have upon the length of survival of patients having a serious chronic disease - cancer.

269. LUNG CANCER AND AIR POLLUTION IN HAMILTON

Sackett, D. L., Shannon, H. S., Charters, J., Cunningham, A. I., Desai, S., Gibson, E. S., McMaster University, Dept. of Clinical Epidemiology & Biostatistics, *1200 Main St. W., Hamilton, Ontario*, L8S 4L8, Canada

Previous work has shown that crude lung cancer death rates are higher in areas of Hamilton nearer to the major industries, but such factors as age, sex, smoking and socio-economic status were not taken into account. This study will make use of data on air pollution levels and age-, sex- and socio-economic-specific death rates as well as a survey of smoking habits to examine roughly 600 lung cancer deaths in the city between 1972 and 1976. After allowing for the confounding variables, the relationship between air pollution and lung cancer mortality will be determined.

270. STATISTICAL ANALYSIS OF PUBLISHED EPIDEMIOLOGICAL STUDIES ON ATMOSPHERIC POLLUTION AND LUNG CANCER

Misfeld, J., Technische Universitat Hannover, Institut fuer Mathematik, *Welfengarten 1, D3000 Hannover, Niedersachsen, Federal Republic of Germany*

Epidemiological studies which examine the relationship between atmospheric pollution and lung cancer are being carried out and the results analyzed statistically.

271. FREQUENCY OF BRONCHIAL CARCINOMA IN RURAL AND AIR-POLLUTED AREAS

Ulmer, W. T., Kammler, E., Silicosis Research Inst., *Hunscheidtstrasse 12, 4630 Bochum, Federal Republic of Germany*

In the last five years all cases of deaths in Bochum, Brilon and Meschede have been investigated. All relatives of persons who died from bronchial carcinoma, liver cirrhosis and apoplexy were visited by a team of investigators and questioned about occupational exposures, main residence and smoking habits of the deceased. Data collection has been completed and statistical analyses are now being carried out.

B. WATER POLLUTION

272. RELATION BETWEEN CANCER RATES AND SOURCE OF DRINKING WATER

Cech, I., Holguin, A., Bradshaw, B., Lee, E. S., Littell, A. S., Stallones, R. A., University of Texas, Health Science Center at Houston, School of Public Health, Dept. of Environmental Sciences, *6515 Freeman, Houston, Texas*, 77025, United States of America

One of the most controversial issues of concern to public health and water resources personnel is the relation between drinking water and cancer. This problem was highlighted when Robert Harris of the Environmental Defense Fund reported that higher rates of total cancer, cancer of the urinary system and of the gastrointestinal tract were observed among individuals drinking treated surface water from the Mississippi River in Louisiana, New Orleans area, compared to others, drinking ground water in the same state. Significant, however, has been the rapid shift from the basic issue, i.e., is the difference observed in cancer rates among the users of different water supplies limited to Louisiana or is it initial evidence of a more general phenomenon? Apparently the Louisiana observation has been accepted as a causal association, since focus has shifted to a search for the particular water contaminant(s) responsible for the observed differences, specifically, to the health risk from waterborne chloro-organic compounds, some of which were shown to be a product of chlorine-disinfection process.

Although evaluation of the health risk of water chlorination has merit, the narrowing of the entire research focus to the matter of chlorination has been hasty. If the observations in Louisiana hold true in other areas, they increase the likelihood of the existence of a water related causal factor which may well be other than chlorination. The fact is, however, that the evidence of the link between cancer and source of drinking water is insufficient for acceptance. A promising and appropriate line of investigation would be to examine this basic issue critically and thoroughly by analyzing cancer mortality rates among the users of both categories of water supplies. The objective of this proposal is to examine cancer mortality and patterns of water utilization in Texas, and to assess the cancer risk in populations using surface and ground sources of drinking water within and among Texas' 254 counties, with geographic references to specific river basins and major ground water aquifers from which the supply is derived.

BIBLIOGRAPHIC REFERENCES: Temporal Variations of Trihalomethane Content of Drinking Water, by Virginia L. Smith, Irina Cech, James H. Brown, and Gregory F. Bogdan. Accepted (November 1979) by J. of Environmental Sciences and Technology.

273. A CASE-CONTROL STUDY OF CHLORINATED DRINKING WATER AND CANCER

Lynch, C. J., Enviro Control Inc., *11300 Rockville Pike, 1 Central Plaza, Rockville, Maryland*, 20852, United States of America

OBJECTIVE: The objective of this project is to determine if consuming chlorinated drinking water is a risk factor for the development of respiratory cancer in the presence of other known risk factors, such as smoking and occupational exposures.

APPROACH: This project is part of a large ongoing NCI case-control study of lung cancer and cigarette smoking that is managed by Enviro Control. Additional data being collected to answer the water chlorination question include water consumption data, residence history, occupational exposure history and water utility information. The relative risk associated with chlorinated drinking water exposure will then be determined after stratifying for tobacco consumption.

PROGRESS: Interviewing has been ongoing at all 6 study sites for three months. Collection of water utility data is under way.

274. CANCER AND DRINKING WATER QUALITY IN NORTH CAROLINA

Struba, R. J., Shy, C. M., Cordier, S. E., University of North Carolina, Chapel Hill Campus, School of Public Health, Dept. of Epidemiology, *Rosenau Hall, 201H, Chapel Hill, North Carolina*, 27514, United States of America

In this study 3,000 cancer cases and an equal number of frequency matched non-cancer controls were compared on several aspects of drinking water quality. Sites examined were colon, rectum and bladder; matching criteria were age, race, sex and geophysical region. Data sources were state mortality, and state and regional water supply statistics. The water systems were characterized on the basis of source, type of chlorination, and presence of upstream pollution (previous use) for the 1960 time period. Urban residence, occupation and socio-economic status are also being controlled in the analysis. Preliminary results show small and significant odds ratios for all three sites (especially bladder and rectum) for treatment, source, and previous use.

275. CASE-CONTROL STUDY OF GASTROINTESTINAL AND URINARY TRACT CANCER MORTALITY IN RELATION TO DRINKING WATER CHLORINATION

Alavanja, M. C., Kupchik, G., City University of New York, Hunter College, School of Health Sciences, Environmental Health Sciences Program, *105 E. 106th St., New York, New York*, 10029, United States of America

Based on previous research which indicated that females residing in areas with chlorinated water had higher risks of dying of gastrointestinal and urinary tract cancer than their counterparts receiving non-chlorinated water, a case-control mortality record study has been initiated in 19 stable New York counties, to see if gastrointestinal and urinary tract cancer mortality can be related to urban or rural residence, mean income, population density, raw water quality, pH, nitrate concentration and color of the water provided for consumption.

276. EPIDEMIOLOGIC STUDY OF BRAIN TUMORS IN A POPULATION EXPOSED TO CHLORINATION BY-PRODUCTS

Greathouse, D. G., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research

Lab., *5555 Ridge Ave., Cincinnati, Ohio,* 45268, United States of America

OBJECTIVE: Assist the prinicipal investigator of a cooperative agreement in the development of a study protocol to investigate the role of chlorination by-products in the development of brain tumors.

APPROACH: Participate in planning and review meetings.

277. CANCER MORTALITY AND WATER FLUORIDE

Cook, P. J., University of Oxford, Dept. of Social & Community Medicine, *S. Parks Rd., Oxford OX2 6HE, England, United Kingdom*

The age-standardized death rates for 'all malignant neoplasms' are being compared for the population of Birmingham (fluoridated in 1964) and the six other towns in England with a population over 400,000 (not fluoridated). Rates are being calculated for the periods 1959-63; 1969-73; and 1974-77. Allowance is being made for boundary changes which, if ignored, would invalidate comparison of the time trends. The situation in Birmingham is being considered in the context of studies comparing fluoridated and non-fluoridated populations in other countries because of the impossibility of drawing any etiological conclusions from a study of one 'affected' population. More detailed time comparisons by individual site and type of cancer are planned when unpublished data have been prepared by the Office of Population Censuses and Surveys. The latter will also permit geographical comparisons between the cancer mortality rates in all areas of England and Wales fluoridated before 1969 and eight neighboring control areas.

278. FLUORIDATION AND CANCER MORTALITY IN NEW ZEALAND

Foster, F. H., Goodall, C. M., New Zealand Dept. of Health, National Health Statistics Centre, *P.O. Box 6314, Te Aro, Wellington, New Zealand*

Cancer mortality in 1961 and in 1976 is being reviewed in two population groups in New Zealand served by fluoridated and unfluoridated public water supplies. The two population groups in 1961 numbered 460,000 (fluoridated) and 225,000 (unfluoridated) from which respectively 850 and 425 cancer deaths were registered. The 1976 populations were 600,000 (fluoridated) and 270,000 (unfluoridated) and cancer deaths were respectively 1,000 and 550. Analysis continues.

279. CANCER MORTALITY AND DRINKING WATER QUALITY

Wigle, D. T., Toft, P., Mao, Y., Johansen, H., Canadian Dept. of National Health & Welfare, Lab. Centre for Disease Control, *Tunneys Pasture, Ottawa, Ontario,* K1A 0L2, Canada

Cancer mortality rates by sex and site for 104 municipalities will be correlated with water quality. Water samples have been analyzed to determine concentrations of the following: amphibole asbestos, chrysotile asbestos, trihalomethanes, total organic carbon, nitrilotriacetic acid, lead, cadmium, zinc, copper, calcium, magnesium and total hardness. For most municipalities, mortality data are available for at least the past 20 years. Cancer and other disease mortality rates will be correlated with the water quality data listed above plus other factors (year of fluoridation, source of water).

280. HEALTH EFFECTS FROM INGESTION OF ASBESTOS FIBERS IN A MUNICIPAL WATER SUPPLY

Sigurdson, E. E., Mandel, J., McHugh, R., Levy, B., Michienzi, L., State Dept. of Health, Disease Prevention & Control Section, *717 Delaware St. S.E., Minneapolis, Minnesota,* 55440, United States of America

The study established baseline incidence of cancer of all sites in the resident population of Duluth, Minnesota, (1970 population 100,078) during the period 1969-1971 and will continue to monitor incidence through 1981 or longer. The purpose of the study is to determine the health effect, if any, on the basis of the investigation of asbestos (amphibole) fibers present in the city water supply during approximately 15 years. Data are collected in the same manner as during the Third National Cancer Survey and compared with the Minneapolis St. Paul component of the Survey and the Surveillance, Epidemiology and End Results Program of the U.S. National Cancer Institute. Additional information will be obtained on cancer cases of selected sites and matched controls. Incidence data for gastrointestinal sites and lung will be published in Environmental Research.

281. ASSESSMENT OF HEALTH IMPACT OF FILTERING ASBESTIFORM FIBERS IN DULUTH

Sigurdsen, E., State Dept. of Health, *717 Delaware St. S.E., Minneapolis, Minnesota,* 55440, United States of America

OBJECTIVE: Determine the relationship - or document the lack of one - between asbestiform fibers in the water supply and cancer.

APPROACH: Gather incidence data on cancer in the population of Duluth, Minnesota and compare with cancer rates in the Minneapolis-St. Paul component of the National Cancer Survey to test whether exposure to asbestiform fibers in the drinking water may contribute to the cancer rate.

PROGRESS: Data collection in progress, analysis of 1969-1974 gastrointestinal cancer incidence data did not show any definite relationship between ingesting asbestiform fibers and cancer. The long latency period between exposure and cancer for asbestos necessitates ongoing surveillance.

282. CANCER INCIDENCE IN RELATION TO ASBESTOS IN DRINKING WATER IN THE PUGET SOUND REGION

Polissar, L., Weiss, N., Fred Hutchinson Cancer Research Center, Program in Epidemiology & Biostatistics, *1124 Columbia St., Seattle, Washington,* 98104, United States of America

A high level of asbestos, occurring naturally, has been found in drinking water in Seattle, Everett, and other nearby areas. Cancer incidence and mortality rates for areas with different water supplies will be calculated. Control factors will include age, sex, race, and socio-economic status. Sites of interest are respiratory tract, gastro-intestinal tract, mouth and esophagus, pancreas, and urinary tract. Other control sites will be examined throughout the analysis. We are also starting a case-control study with interviews conducted in the high exposure area.

283. ACCIDENTAL EXPOSURE TO CHROMIUM

Matos, E. L., Urquijo, C., Marengo, A. J., Instituto Oncologia Angel H. Roffo, Section of Chemical & Environmental Carcinogenesis, *Av. San Martin 5481, 1417 Buenos Aires, Argentina*

A series of studies shows an increase in cancer incidence among workmen taking part in chromates manufacture, just as in vitro studies demonstrate an increase in chromosomal aberrations and sister chromatid exchange in cells treated with hexavalent chromium. The maximum level of hexavalent chromium in running water approved by WHO is 50 micrograms/kg. In San Martin District, Buenos Aires, the water-table used by the inhabitants neighboring a plating works was found to be contaminated. The levels of hexavalent chromium measured in the water wells were higher than 5 mg/kg. Several months ago these inhabitants presented symptoms of poisoning in respiratory, digestive and urinary systems and skin. 208 persons, who live in the same block as the industry, will be followed up for cancer of different sites. The mortality rates for the general population will be used as a control for the cancer death rate.

284. STUDIES OF DRINKING WATER QUALITY AND CANCER IN IOWA

Isaacson, P., Bean, J., Jordan, J., University of Iowa, School of Medicine, Dept. of Preventive Medicine & Environmental Health, *Jessup Hall, Iowa City, Iowa,* 52240, United States of America

OBJECTIVE: The basic objective is to use the extensive data and information resources of Iowa to further examine the human cancer risks associated with drinking water quality. In particular, the research effort will include assessments of the cancer risks associated with nitrates, radioactivity (radium 226), and energy related production by-products in drinking water.

APPROACH: Populations will be defined, or classified, into groups of similar exposure based on general or specific water quality factors. Within the defined groups, the population will be stratified by sex and community size. Actual and expected age adjusted cancer incidence rates will be computed for each subgroup. Incidence ratios (observed frequency/expected frequency) will be compared among comparable subgroups.

PROGRESS: Much of the available water quality data has been computerized; special purpose computer programs have

been written; and preliminary assessments of cancer risks have been completed.

285. GEOCHEMICAL ENVIRONMENT AND OCCURRENCE OF MALIGNANT TUMORS IN SELECTED DISTRICTS OF CZECHOSLOVAKIA

Jilek, V., Thurzo, V. A., Plesko, I., Inst. of Mineral Raw Materials, Dept. of Technology, *Vitezna 425, Kutna Hora 28403, Czechoslovakia*

The chemical composition and radioactivity of drinking waters in selected districts of Czechoslovakia are being studied in relation to the observed differences in the occurrence of malignant tumors. Maps will be made using the data obtained, the amounts of chemical elements ingested by the population calculated and the relation between the geochemical environment and mortality from malignant tumors evaluated statistically. The levels of some trace elements in selected organs of the human body (necropsy material) will be determined by neutron activation analysis and atomic absorption spectrophotometry.

286. GASTRIC CANCER AND NITRATE INGESTION - NITRATE IN DRINKING WATER

Fraser, P. M., Chilvers, C. E., Beral, V. S., Hill, M. J., University of London, London School of Hygiene & Tropical Medicine, Dept. of Epidemiology & Medical Statistics, *Keppel St., London WC1E 7HT, England, United Kingdom*

Evidence is accumulating that populations ingesting large amounts of nitrate have a high mortality from cancer, particularly of the stomach, due to the formation in vivo of carcinogenic nitrosamines. Nitrate levels in some water sources in the eastern regions of England are rising steadily due to extensive use of fertilizer. Mortality from gastric cancer within these regions in the years 1969-73 is being examined in relation to the nitrate concentration in drinking water 15 to 20 years previously. The objectives of this study are: 1) to establish whether there is an increased risk of gastric cancer in populations exposed to moderately high levels of nitrate in drinking water and 2) to determine a safe level for nitrate in drinking water.

287. EPIDEMIOLOGICAL FACTORS IN GASTRIC CANCER, CLUJ DISTRICT, ROMANIA

Bolba, G., Bara, A., Karacsony, Z., Ciurdareanu, S., Ignat, I., Junie, E., Oncological Inst. of Cluj-Napoca, Dept. of Epidemiology & Statistics, *Republicii Nr. 34-36, R3400 Cluj-Napoca, Romania*

Study of cancer incidence in the Cluj district (1974-1975) shows that in males gastric cancer is the most common form of cancer (42.2 per 100.000 per annum) being more widespread in the rural areas (about 73.0). In females, breast cancer is the most common form of cancer (27.0) followed by cervix uteri (23.8) and stomach (22.1). Previously, the rank order was cervix uteri, stomach, cancer. The correlation between nitrosamines and gastric cancer is being studied, estimating the secondary amines in traditional foodstuffs and the nitrate and nitrite in drinking water in rural areas. Routine systematic investigations of pollution in drinking water in the Cluj district show considerable variations.

288. A RETROSPECTIVE STUDY OF CANCER IN RELATION TO A SPECIFIC ENVIRONMENTAL FACTOR (WATER NITRATE)

Lumholtz Frederiksen, P., Conrad, C., Jensen, O. M., KAS Herlev, Dept. of Radiotherapy & Oncology, *Herlev Ringvej, 2730 Herlev, Denmark*

The incidence of testis cancer in Denmark has for years been known to exceed that of neighboring countries (6.0 new cases/year/100,000 males). In this study a small, geographically limited 'hot-spot', possibly of recent origin, with an incidence of 31.7 new cases/year/ 100,000 males during the last 2 years (01/06/76 - 01/06/78) has been detected. This particular region differs from the rest of the island of Sjaelland (the island where the capital city of Copenhagen is situated) in one specific respect: the content of nitrate in deep ground-water supplies. The possibility of the formation of carcinogenic nitrosamines from nitrate, nitrite and secondary amines in humans is being examined. Data are now being collected to see if there is a significant rise in the incidence in other parts of the country.

289. NITRATE LEVEL IN DRINKING WATER AND GASTRIC CANCER

Juhasz, L., Hill, M. J., Nagy, G., Szabolcs Szatmar County Hospital, Policlinic Unit, *44 Voeroeshadsereg u. 68, H4401 Nyiregyhaza, Hungary*

Stomach cancer is very common in Hungary. Shallow well water in the County Szabolcs-Szatmar very often has a high nitrate content. As part of a larger study the possible relationship between incidence of stomach cancer, nitrate level of drinking water, occurrence of methemoglobinemia cases and geographical distribution by soil types is examined. This analysis and comparison of Hb-values of pregnant women from the year 1975 onwards is in progress. Analyses of urine from selected places will be performed in the Bacterial Metabolism Research Laboratory, London. The first results were presented at the 6th IARC Meeting on Analysis and Formation of N-Nitroso Compounds, 16-21 October, Budapest, Hungary, and will be published shortly.

290. STOMACH CANCER AND NITROSAMINES

Juhasz, L., Hill, M. J., Nagy, G., Marton, M., Cancer Registry of the County Szabolcs Szatmar, *68 Voroshadsereg Str., H4401 Nyiregyhaza, Hungary*

OBJECTIVE: To study the supposed relationship between stomach cancer and nitrosamines.

APPROACH: 1) To collect data on nitrate content of water of wells from each village and town of the county. 2) To make a map indicating the distribution of patients with stomach cancer in the county (1952-1976). 3) To make a map showing the distribution of cases with methemoglobinemia in the county. 4) To compare the data mentioned under points 1, 2, and 3. 5) Analysis of nitrosamine content of village water (by Hill's Laboratory of Bacteriology, London).

PROGRESS: We are working now on points 1, 3 and 4.

291. RELATIONSHIP BETWEEN LEVELS OF NITRATE IN DRINKING WATER AND CANCER MORTALITY

Scragg, R. K., Commonwealth Scientific & Industrial Research Org., Division of Human Nutrition, *Kintore Ave., Adelaide, S. Australia 5000, Australia*

Environmental nitrates in water, by their bacterial conversion to nitrosamines, are thought to be associated with an increased mortality from cancer, especially stomach cancer. The Southeast of Australia, in particular the State of Victoria, has communities with high levels of nitrate in their drinking water. The type-specific mortality rates for all cancers are being compared in the high and low water nitrate areas of rural Victoria.

292. CORRELATION OF WATER TRIHALOMETHANE LEVELS IN SELECTED CITIES WITH CANCER MORTALITY

Canter, K., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio,* 45268, United States of America

This project involves statistical correlation of available data on trihalomethane levels in water with age- and sex-adjusted site-specific cancer mortality data. The water was that collected during the 80 city National Organic Reconnaissance Survey supported by the Environmental Protection Agency (EPA), the National Organic Monitoring Survey (113 cities) and the EPA Region V Survey. The mortality statistics were those supplied by the National Center for Health Statistics to the National Cancer Institute.

293. EPIDEMIOLOGIC STUDY OF BLADDER CANCER RISK ASSOCIATED WITH TRIHALOMETHANES IN DRINKING WATER

Canter, K., Hoover, R., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio,* 45268, United States of America

OBJECTIVE: To assess the bladder cancer risks associated with exposure to purgeable organics in drinking water.

APPROACH: Include exposure to purgeable organics as one of the risk factors to be evaluated as part of the large National Cancer Institute supported study of bladder cancer and saccharine usage.

PROGRESS: All of the cases and controls have been interviewed, much of the historical water supply and water

quality data has been abstracted, and the water sampling and analysis effort is well underway.

294. CASE-CONTROL STUDY OF WATER QUALITY AND CARCINOGENESIS IN PENNSYLVANIA

Bahn, A., Greathouse, D. G., University of Pennsylvania, School of Medicine, Dept. of Community Medicine, *36th & Hamilton Walk, Philadelphia, Pennsylvania*, 19174, United States of America

This is a case-control retrospective study of colon cancer in four counties - Philadelphia, Delaware, Chester, and Bucks - of Pennsylvania. Decedent cases (colon cancer) and controls (deaths due to causes other than cancer) will be drawn from the state mortality records and the next-of-kin listed on the death certificates will be interviewed. Live cases will be selected from hospital records and controls will be randomly selected from the counties. For each case and control information will be obtained concerning residence, occupation, and medical histories, smoking habits, dietary patterns and medicine usage. Detailed chacterization of water sources, treatment methods and chemicals will be obtained. Relationship(s) between routine water analyses and the detailed organic analyses will be investigated for use in historical extrapolation of specific organic contaminant levels in the water. A further major goal of the project is to investigate and compare alternative case-control study methods. Effectiveness of using next-of-kin of decedents for determining relevant exposure will be compared with the use of live cases. Effect of time between death and interview in reliability and usefulness of data will be evaluated. The methodological information obtained will be useful in future investigations of the role of water constituents in the development of chronic diseases.

295. RELATIONSHIP OF ORGANIC CONTAMINANTS IN DRINKING WATER TO CANCER MORTALITY AND MORBIDITY IN CONNECTICUT

Woodhull, R. S., Jarema, R., Meigs, W., State Dept. of Health Services, *79 Elm St., Hartford, Connecticut*, 06115, United States of America

OBJECTIVE: This study will provide the necessary data on drinking water supplies in Connecticut to determine the relationship between (1) type of water supply and drinking water cancer and mortality over time and (2) organics in drinking water and the incidence of bladder cancer.

APPROACH: This objective will be accomplished through two studies: (1) Drinking water and cancer mortality - This study will utilize existing drinking water data for the state of Connecticut along with newly collected data for comparison with the tumor registry. (2) Bladder cancer study - This study is part of a large scale EPA bladder cancer study. It will be a case-control study using 540 cases and 1080 controls selected in Connecticut. Questionnaires will be given and water samples will be collected for chemical analysis.

296. HEALTH IMPACTS OF ALTERED GEOCHEMISTRY ASSOCIATED WITH MINE DRAINAGE FROM WESTERN INTERIOR COALS

Wixson, B. G., Gale, N. L., Pottinger, H. J., University of Missouri, Rolla Campus, School of Engineering, Dept. of Civil Engineering, *Rolla, Missouri*, 65401, United States of America

OBJECTIVE: This study is designed to determine the existence of a relationship between acid mine drainage contamination of potable water supplies and human health. This is to be done in the western interior coal region encompassing the states of Missouri, Iowa, Oklahoma, and Kansas.

APPROACH: The approach is through an ecologic study looking for relationships between epidemiologic data and water quality data. The epidemiologic data include county cancer mortality rates for 30 causes of death from NCI and census information. Water quality data include surface and ground water quality data and data obtained from samples of tap water.

297. WATER SOURCES AND CHARACTERISTICS AND RISK OF MALIGNANCIES OF SELECTED SITES IN SELECTED LOUISIANA PARISHES

Gottlieb, M. S., Tulane University of Louisiana, School of Medicine, Dept. of Biostatistics & Epidemiology, *1430 Tulane Ave., New Orleans, Louisiana*, 70112, United States of America

In order to determine whether certain drinking water sources predispose individuals to cancer, deaths from cancer of selected sites will be matched to control deaths from non-cancer (non-related causes) within groups of selected parishes with similar characteristics except having differing water sources (river and ground). Matching will be for age, sex, race, and year of death. Cases and controls will be characterized by place of birth, ancestry (Acadian or otherwise), water source and characteristics, occupation and industry, and distance from industry. Length of time on water source for individuals will be determined from residence data, characteristics of the water during the last ten years of life, as well as distance of the residence from local industries characterized by type, size and length of exposure time. These factors will be compared for cancer deaths and non-cancer deaths to determine the contribution of single and multiple variables to the likelihood of dying from cancer. An incidence study will follow for selected sites and parishes where the mortality risk is high. This will be followed by a case/control interview study, including carcinogen screening for selected parishes at high risk for selected sites.

298. COMPARE OCCURRENCE AND LEVELS OF DRINKING WATER CONSTITUENTS AMONG 12 MATCHED PAIRS OF HIGH AND LOW CANCER MORTALITY COUNTIES (ABBREV)

Greathouse, D. G., Michael, G., Kraemer, D., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio*, 45268, United States of America

OBJECTIVE: The aim of this project is to determine if matched counties with contrasting cancer mortality rates use drinking water that differs significantly in terms of occurrence and levels of contaminants, treatment technologies used, and/or source type (ground or surface).

APPROACH: Twelve pairs of matched counties were selected; matching criteria were region of the country, avg. educational level, percent of the population employed in the manufacturing industry, percent urbanization, total population years at risk. Within each pair, one county had a high and the other a low mortality rate for females due to colon, rectum, bladder, and liver cancer. Historical water quality and treatment information were collected for performance. Extensive water analyses were performed; analysis included determinations for 40 inorganics, trihalomethanes, TOC, fluorescence, asbestos, radionuclides, and mutagens.

PROGRESS: The field work has been completed and all water samples have been analyzed. Most of the data has been computerized. It is anticipated that the data analysis effort will begin by October 1, 1979 and be completed by March 31, 1980.

299. DRINKING WATER QUALITY AND COLON CANCER

Ibrahim, M. A., Struba, R. J., Shy, C. M., University of North Carolina, Chapel Hill Campus, School of Public Health, Dept. of Epidemiology, *Rosenau Hall, 201H, Chapel Hill, North Carolina*, 27514, United States of America

This study investigates the relationship of drinking water quality to cancer of the colon in North Carolina using the case-control approach. A series of living colon cancer cases and a matched series of hospital controls will be compared for differences in quality of their drinking water and other environmental factors. A substudy will determine whether past diet is a confounding factor. Sample size and methodology have been chosen to detect small differences in risk, and water quality indices have been constructed for periods 20 and 30 years in the past to account for the issues of latency. These indices, which are based on source, treatment and prior use characteristics, provide a basis for establishing a gradient of carcinogenic exposure. With this information, estimates of risk for each exposure level will be obtained and comparisons between these will be made. Using the rigorous approach, it will be possible to provide meaningful data on the importance of water borne carcinogens in the etiology of a leading cancer site.

300. EPIDEMIOLOGICAL STUDIES OF THE RELATIONSHIP BETWEEN RE-USE OF WATER AND HAZARDS TO HEALTH

Beresford, S. A., Ives, K. J., Packham, R., University of London, Royal Free Hospital School of Medicine, Dept. of Clinical

Epidemiology & Social Medicine, *8 Hunter St., London WC1N 1BP, England, United Kingdom*

The aim of the studies is to investigate the effects on the health of populations of drinking water derived from water sources contaminated with domestic and industrial waste, with particular reference to cancer of the digestive system, and of the genitourinary system. The first stage of the studies is to examine the association between cancer mortality and the source of water supply in terms of the history of pollution and degree of re-use. The hypothesised association arises mainly from the Mississippi River study although other studies have also examined this association. Possible disease outcomes other than cancer will also be investigated to provide a basis for formulating further hypotheses.

301. ENVIRONMENTAL INFLUENCES ON CANCER MORBIDITY IN THE PITTSBURGH REGION

Andelman, J. B., Greathouse, D. G., University of Pittsburgh, Graduate School of Public Health, Dept. of Industrial Environmental Health Sciences, *4200 5th Ave., Pittsburgh, Pennsylvania,* 15260, United States of America

This project involves the use of regression modelling techniques to determine if there are differences in cancer morbidity rates for water supplies (including sources and source types) which cannot be explained by available information concerning socioeconomic status, housing density, industrialization, etc. Specifically, the Third National Cancer Survey cancer morbidity data for 19 different anatomical sites are being regressed against census tract data aggregated by water utility service areas. Residuals from these regressions are cross-classified separately with water service areas, water sources, and water source types to determine if the residuals are independent of these major water classifications.

302. A STUDY OF CANCER AND THE PUBLIC DRINKING WATER SUPPLIES IN MISSOURI

Marienfeld, C., McCabe, L., Collins, M., Rust, P., Bartling, G., Wright, H., Shoop, G., Reddy, R., Tsutakawa, R., Miller, R., University of Missouri, Columbia Campus, School of Medicine, Dept. of Community Medicine, *M228 Medical Sciences, Columbia, Missouri,* 65201, United States of America

This project involves setting up a data base of mortality, morbidity, and environmental information for rural postal routes grouped into rural water supply areas. This technique permits comparison of cancer rates for water supply areas which differ considerably in terms of water quality, industrial exposures, geology, and socioeconomic characteristics. County units which are often used may not coincide with water utility service areas. This project should permit an evaluation of the health and environmental (primarily drinking water) consequences of existing or newly established industrial and/or mining operations within rural areas.

303. COMPARISONS OF OCCURRENCE AND LEVELS OF DRINKING WATER CONSTITUENTS AMONG PAIRS OF HIGH AND LOW CANCER MORTALITY COUNTIES IN OHIO

Greathouse, D. G., Reiches, N., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio,* 45268, United States of America

The basic study procedures and goals of this project are similar to those of the national study. As a result of at least two independent epidemiological studies attention has been focused on Ohio because of the high cancer mortality rates for counties supplied with drinking water from surface sources. Since Ohio counties represent wide contrasts in water sources, geology, industrialization, socioeconomic levels, and cancer mortality rates, it was judged that a study limited to Ohio would be worthwhile. The selection of study counties will be based on the county mortality data available from Ohio State University and the industrial data available from the Ohio Environmental Protection Agency and various publications.

304. EPIDEMIOLOGICAL STUDIES ON THE FREQUENCY OF TUMORS IN FISH FOUND IN POLLUTED WATERS AND THOSE FOUND IN UNPOLLUTED WATERS

Brown, E. R., Keith, L. A., Callaghan, O., Greenberg, S., Sinclair, T., Beamer, P. V., University of Health Sciences - Chicago Medical School, Medical School, Dept. of Microbiology, *2020 W. Ogden Ave., Chicago, Illinois,* 60612, United States of America

OBJECTIVE: An ongoing (1967) study to show that the presence of carcinogens in water directly influences the incidence of tumors in fish and mammals (including human beings) utilizing such waters for extended periods.

305. STUDIES OF DRINKING WATER QUALITY AND CANCER IN IOWA

Greathouse, D. G., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio,* 45268, United States of America

OBJECTIVE: To work with Dr. Peter Isacson, principal investigator for cooperative agreement No. R-806301-02, in the design and interpretation of the project entitled 'Studies of Drinking Water Quality and Cancer in Iowa.'

APPROACH: Participation in planning and review meetings.

306. A STUDY OF CANCER AND THE PUBLIC DRINKING WATER SUPPLIES OF MISSOURI

Sonich, C., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio,* 45268, United States of America

OBJECTIVE: To participate with Dr. Marienfeld, principal investigator for coop. agree. No. R-805297-03, in planning for future activities and interpretation of results for the project entitled 'A Study of Cancer and the Public Drinking Water Supplies of Missouri.'

APPROACH: Participation in planning and review meetings.

C. BROAD EPIDEMIOLOGICAL SURVEYS OF ENVIRONMENTAL FACTORS AND CANCER INCIDENCE

307. DETERMINANTS OF CANCER AND CARDIOVASCULAR DISEASE MORTALITY IN ASBESTOS MINING COUNTRIES OF CALIFORNIA

Ziskind, R. A., Hahn, J., Haile, B., Smith, D., Spivey, G. H., Science Applications Inc., Energy Environment Systems Division, *1801 Ave. of the Stars, Suite 1205, Los Angeles, California,* 90067, United States of America

The purpose is to evaluate the association of mortality from respiratory tract cancer, mesothelioma, and cardiovascular disease with length of residence in the proximity of natural asbestos formations and processing activities after controlling for the effects of cigarette smoking, occupation, and genetic susceptibility. The study design will define the geographical bounds and causes of death to be investigated. A questionnaire will be used to obtain information from surviving family members. A comprehensive inventory and characterization of stationary, mobile, anthropogenic and natural sources of asbestos will be made in all case and control areas for the time periods of interest. Air and water exposure maps covering the study areas will be constructed and used to correlate personal histories with degree of exposure.

308. EPIDEMIOLOGICAL ASPECTS OF ASBESTOSIS AND MALIGNANT TUMORS

Yazicioglu, S., Ilcayto, R., Balci, K., Sayli, B. S., Cobanoglu, N., Basaran, N., Demirel, M., Oezdemir, N., Karadede, S., Muhtar, H., Bingoel, R., Degertekin, H., Diyarbakir University, Medical Faculty, Dept. of Chest Diseases, *Diyarbakir, Turkey*

Chrysotile and tremolite asbestos, freely dug, sold and used by inhabitants of some villages and towns in Turkey, leads to pleural calcification with the eventual complication of malignancy of the respiratory tract. This study aims to gather information concerning malignancies of the upper and lower segments of the respiratory tract and, to some extent, of the digestive

system, among people of different socio-economic levels and geographic regions. The biological effects of asbestos will also be investigated in both humans and animals using clinical, experimental and laboratory methods, electron microscopy and mineralogical analysis of the biological material. The groups to be studied are: (1) hospital cases; (2) cases found in screening of the field; (3) animals such as mules and asses (used for transport); (4) laboratory animals such as rats and rabbits. Air and water pollution studies will also be carried out. This study will involve large control groups. Since Turkey is rich in different minerals, this investigation will reveal similar effects, if any, of other elements.

309. ENDEMIC PLEURO-PERITONEAL DISEASE IN RURAL TURKEY

Baris, Y. I., Artvinli, M. O., Sahin, A. A., Savas, T. C., Isiksalan, M., Kolacan, B., Goektepeli, J. A., Hacettepe Universitesi, Faculty of Medicine, Dept. of Chest Diseases, *Ankara, Turkey*

Recent clinical and epidemiological studies in Turkey have revealed that calcified pleural plaques, chronic fibrinous pleurisy and malignant mesothelioma are endemic in some villages with asbestos deposits. Mineralogical electron microscopy studies in airborne dust samples in these villages revealed mostly tremolite, chrysotile asbestos and other mineral fibers (rutile, eckermannite, antigorite etc.). However, there are two villages in the Nevsehir region without asbestos deposits which have a much higher incidence of the same diseases. Mineralogical studies of some geological and airborne dust samples and studies of lung tissues have demonstrated the presence of erionite, a type of zeolite. Part of the study has been published.

310. RISK FACTORS FOR MALIGANT MESOTHELIOMA

Haider, M., Neuberger, M., Raber, A., Eckhardt, S., Universitat Wien, Inst. of Environmental Hygiene, *Kinderspitalgasse 15, 1090 Vienna, Austria*

Morbidity and mortality data from the Austrian cancer register on primary malignant pleural tumors are corrected and completed by query to pathologists and clinicians. So far 192,172 autopsy records have been reviewed. All authenticated cases diagnosed since 1969 in the Austrian population are being analyzed retrospectively with regard to risk factors, especially asbestos exposure. Occupational histories obtained from social insurance schemes are completed with the help of physicians, safety engineers, relatives, fellow workers, etc. In selected cases of deceased patients the dust content of the lung is analyzed. From 1969 to 1974, 116 malignant pleural mesotheliomas were certified, the majority of which had no occupational asbestos exposure. Preliminary results are published in 'New Approaches to Risk Estimation of Air Pollutions,' Facultas, Vienna (1979).

311. ASBESTIFORM MINERALS

Ross, M., U.S. Dept. of the Interior, Geological Survey, Geologic Div., *12201 Sunrise Valley Dr., Reston, Virginia*, 22092, United States of America

OBJECTIVES: Assess the epidemiological, mineralogical, and petrological studies that have been made which can contribute to our knowledge of the role naturally occurring minerals play in the production of lung and intestinal cancer and mesothelioma in the U.S. population. Initiate mineralogic studies which may give an insight into the 'asbestos and health' problem.

312. CONTINUING RETROSPECTIVE STUDY OF ALL CASES OF MESOTHELIOMA IN NORTHERN IRELAND TO DETERMINE THEIR SOURCE OF ASBESTOS EXPOSURE

Langlands, J. H., Bharucha, H., Simpson, M., Belfast City Hospital, Respiratory Investigation Center, *93 Lisburn Rd., Belfast BT9 7AB, United Kingdom*

The objective of this study is to detect sources of asbestos exposure in the community which are sufficient to cause mesothelioma, in order to determine whether preventive measures applied to recognized sources of exposure are sufficient. Arrangements are made for all cases of mesothelioma to be reported to the investigators as soon as possible so as to obtain pathological material for examination after death.

313. PILOT STUDIES OF ENVIRONMENTAL FACTORS AND CANCER MORTALITY

Wilkinson, G. S., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., Population Studies Div., *Research Triangle Park, North Carolina*, 27709, United States of America

These studies are concerned with investigating potential relationships between environmental factors such as presence of asbestos mines or proximity of nuclear and fossil-fueled power plants and mortality from cancer within the United States. Mortality rates for various types of cancer in areas having asbestos mines or power plants are being compared with mortality rates in areas without such sources of potential pollution.

314. CARCINOGENICITY OF ASBESTOS DUST

Donna, A. F., Betta, P. G., General City Hospital of Alessandria, Anatomic & Histologic Pathology Inst., *Via Venezia 18, Alessandria, Italy*

Pleural mesothelioma would appear to have a low overall incidence in Italy. In some regions of the country such as Piedmont, Liguria and Friuli, the incidence is significantly increased, being highest in the district of Alessandria in Piedmont. The aim of the study is to confirm the reported high incidence in Alessandria and to clarify the role of asbestos dust through questioning of individuals about work and environmental conditions, as well as through biopsy or necropsy confirmation of diagnosis.

315. COMPARATIVE STUDY OF CANCER RISKS FROM EXPOSURE TO EFFLUENTS FROM FOSSIL FUELLED AND NUCLEAR POWER STATIONS

Vohra, K. G., Bhabha Atomic Research Centre, Div. of Radiological Protection, *Trombay 400085, Bombay, India*

The future large scale production of nuclear power would involve radiation exposure of larger groups of occupational workers, individuals and groups in the population, and the population at large. In view of the concern about the risks of nuclear power often expressed by uninformed public, it is necessary that the risks associated with alternative energy sources such as those based on fossil fuels are compared with similar risks associated with nuclear energy production.

The risks of cancer mortality from ionizing radiations have been studied by two important international Committees, viz. the United Nations Scientific Committee on the Effects of Atomic Radiations and the US Advisory Committee on the Biological Effects of Ionizing Radiations (BEIR Committee). Extensive epidemiological data on the incidence of cancer is also available for several industrial cities, compiled by a number of research institutes. However there has been very little effort in collecting the data of both types at one institution and comparing the two in terms of quantitative risk evaluation.

The proposed program is concerned with the risks of cancer induction associated with the above two energy sources. The risks of specific cancers, for example, lung cancer, would be compared, based on extensive environmental measurements data and epidemiological data.

Risk analysis for radiation induced cancers will be based on the extensive data available on human exposure and animal experiments. The risk associated with fossil fuelled power stations will be assessed on the basis of available data on selected chemical carcinogens and the epidemiological data for urban areas affected by continuous operation of fossil fuelled power stations. The project will also include some measurements of chemical carcinogens in selected areas for direct comparison with epidemiological data.

316. EPIDEMIOLOGICAL STUDY OF LEUKEMIA IN MESA COUNTY, COLORADO, U.S.A.

Ferguson, S. W., Franz, L., Vernon, T., Cunningham, M., State Div. of Epidemiology & Disease Control, *4210 E. 11th Ave., Denver, Colorado*, 80216, United States of America

This is a descriptive and analytical study in Mesa County, Colorado, USA, where the age-adjusted leukemia incidence rates are 2-2.5 times the expected, based on Colorado and US data (41 observed: 20 expected in 1970-1976). In the 1950s and 1960s tailings for a uranium mill were used extensively in Mesa County for construction - as a backfill under basements and around foundation walls. For the analytical study the case-control approach is used. Leukemia patients, patients with other

malignancies believed associated with ionizing radiation and patients with cardiovascular disease are interviewed. Work over the past year has confirmed the leukemia excess, but has not shown a direct association with residences containing uranium mill tailings.

317. NATURAL BACKGROUND RADIATION AND CANCER FREQUENCY IN HUMAN POPULATION GROUPS

Allwright, S. P., Kevany, J. P., Doherty, M., McAulay, I. I., University of Dublin Trinity College, St. James Hospital, Dept. of Community Health, *James St., Dublin 8, Ireland*

Studies investigating the relationship between natural radiation and cancer have produced varying and inconclusive results. The objective of this study is to determine type specific age standardized cancer death rates in Ireland in relation to defined areas of high and low background radiation. Regions of probable high and low radiation have been selected on the basis of existing geological data. Radiation levels, both indoor and outdoor, in these areas will be monitored. The unit area for radiation monitoring will be ten sq km, based on the National Reference Grid. Cancer mortality in the regions where radiation has been measured will be determined, also based on the ten sq km unit of area.

318. BACKGROUND RADIATION AS A CARCINOGENIC HAZARD

Frigerio, N. A., Stowe, R. S., Argonne National Lab., Radiology Group, *9700 S. Cass Ave., Argonne, Illinois*, 60439, United States of America

OBJECTIVES: To compare cancer incidence and mortality rates with background radiation levels in various regions of the world. Comparisons include components of background radiation, and all the various types of malignancies and anatomical sites.

319. CANCER INCIDENCE AND EXPOSURE TO NATURAL IRRADIATION

Masse, L. M., Pincet, J., Gallou, M., Tallua, B., Ecole Nationale de la Sante Publique, Dept. of Statistics, *Ave. du Prof. Leon Bernard, 35043 Rennes Cedex, France*

Incidence of cancer by village according to the level of natural irradiation.

320. MORTALITY AND CANCER MORBIDITY IN AN AREA SURROUNDING AN ARSENIC EMITTING SMELTERY

Pershagen, B. G., Elinder, C. G., Bolander, A. M., Karolinska Institutet, Dept. of Environmental Hygiene, *Solnavagen 1, Box 60400, S10401 Stockholm 60, Sweden*

The purpose of the investigation is to determine whether an increased mortality and/or cancer morbidity exists in an area around the Roennskaersverken smelter works in northern Sweden. Founded in 1928, this metallurgical plant, processing mainly non-ferrous metals, has, since the start of operations, used ore with a high arsenic content. This has resulted in pollution of air and water by arsenic as well as by other metals and sulphur dioxide. The investigation is in the form of a cohort study. The exposed comprise the population of two parishes in the vicinity of the plant, defined from the National Census in 1960. A reference population in the same part of Sweden with a similar degree of urbanization, occupational profile and age distribution was chosen. The causes of death and cancer morbidity for the two populations are to be followed up over a period of 14 years. Results from a pilot study have shown a significantly higher mortality rate for lung cancer in men in the exposed area. However, this increase was no longer significant when the occupationally exposed at Roennskaersverken were excluded. The latter showed a highly significant excess mortality from primary respiratory cancer. The smoking habits in the two populations will be studied using a case-control method.

321. EPIDEMIOLOGICAL STUDIES OF CANCER

Caldwell, G. G., Heath, J., Falk, H. L., Zack, M. M., Stein, G., Kreiss, K., Ing, R., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, Bureau of Epidemiology, Cancer Branch, *1600 Clifton Rd. N.E., Atlanta, Georgia*, 30333, United States of America

Various projects are being conducted: 1) A case - control study of interpersonal contact as a risk factor for leukemia/lymphoma in the Metropolitan Atlanta area: 2) laboratory epidemiological studies of families owning cats shedding feline leukemia virus (in collaboration with several tumor virus laboratories in the USA; 3) ad hoc field investigations of community clusters particularly leukemia/lymphoma; 4) retrospective assessment of leukemia risks among persons exposed to atmospheric atom bomb tests in the US in 1957 (in collaboration with other Federal groups); 5) prospective assessment of possible cancer risk in Michigan residents ingesting polybrominated biphenyl in 1973-74 (in collaboration with the State of Michigan and various Federal groups); 6) a follow-up study of women who have died of carcinoma of the cervix to determine whether or not the disease was potentially preventable.

322. POSSIBLE INFLUENCE OF ENVIRONMENTAL POLLUTION ON CANCER MORTALITY IN A POPULATION LIVING NEAR A VINYL CHLORIDE POLYMERIZATION PLANT

Theriault, G. P., Iturra, H., Bourbonnais, R., Universite Laval, School of Medicine, Dept. de Medecine Sociale et Preventive, *Ste. Foy, Quebec*, G1K 7P4, Canada

This retrospective case-control study aims to determine whether exposure to a factory environment accounts for higher death rates in the population of Shawinigan, Quebec, where vinyl chloride polymerization plant is located. All men aged 25-64 who died from cancer in Shawinigan between 1965 and 1974 will be examined for occupational history, duration of residence in Shawinigan, place of residence there and alcohol and tobacco consumption; they will then be compared with men of similar age who lived in Shawinigan and died at the same time from another cause.

323. MALIGNANT MELANOMA AND ENVIRONMENTAL EXPOSURE

Aldrich, T. E., University of Miami, School of Medicine, Dept. of Epidemiology & Public Health, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida*, 33152, United States of America

The summary for this project is under entry no. 203.

324. EPIDEMIOLOGICAL AND ETIOPATHOGENIC STUDY OF TUMORS OF SEROUS SURFACES

Donna, A. F., Betta, P. G., General City Hospital of Alessandria, Institute of Pathology, *Via Venezia 18, Alessandria, Italy*

During a survey of mesotheliomas in the district of Alessandria with special regard to their relationship with exposure to asbestos, a preponderance of these tumors was reported in people living in the countryside. Occupational histories obtained from these patients and/or their relatives and environmental surveys do not indicate any relationship between these tumors and exposure to asbestos. The object is to establish whether some chemicals (nitrogen and cyanide organic compounds), widely used in the Alessandria countryside, are carcinogenic in the serous membranes. This hypothesis is being assessed, at the same time, by a middle-term treatment of mice, and the mutagenic properties of the chemicals may also be examined.

325. EPIDEMIOLOGY OF GASTRIC CANCER AND PRECURSOR LESIONS

Correa, P., Tannenbaum, S., Haenszel, W. M., Cuello, C., Montes, G., Louisiana State University, Medical Center, School of Medicine, Dept. of Pathology, *1542 Tulane Ave., New Orleans, Louisiana*, 70112, United States of America

The possible relation between nitrites in the environment and gastric carcinogenesis is being investigated. Nitrites and nitroso compounds are being estimated in the gastric juice and in local foods of the population of Narino, Colombia, where a high prevalence of gastric cancer and precursor lesions has been found. The role of chronic atrophic gastritis in carcinogenesis is being investigated in prospective studies of the population.

326. STUDY OF ENVIRONMENTAL CARCINOGENS

Nemenko, B. A., Moldakulova, M. M., Kazakhskiy Nii Onkologii i Radio., Laboratory of Carcinogenic Agents of the Environment, *Abai 91, Alma Ata 480072, Kazakh S S R, Union of Soviet Soc. Republics*

The relationship between the level of environmental pollution with benzo(a)pyrene, zinc, cadmium, lead, beryllium, ar-

senic, and selenium and lung cancer incidence among workers and citizens is being investigated in a large plant of ferrous metals.

327. RELATION BETWEEN URBAN AND INDUSTRIAL FACTORS AND MALIGNANT NEOPLASMS IN AN UPPER SILESIAN CITY

Zemla, B., Kolosza, Z., Inst. of Oncology, Cancer Epidemiology Unit, *Armii Czerwonej 15, 44100 Gliwice, Poland*

The city of Zabrze has been divided into ten districts differing in level and character of industrialization. Correlations are made between stomach and lung cancer incidence in native and migrant populations, classified by sex, age, residence, and quality of water supply (including hardness, content of nitrite, nitrate, iron, magnesium, manganese, silicon), as well as air pollution, mainly levels of aromatic hydrocarbon emissions, and other environmental factors.

328. RELATION BETWEEN ENVIRONMENT AND CANCER

Rylander, C. R., Axelsson, G., Goteborgs Universitet, Dept. of Environmental Hygiene, *411 Vasaparken, S40010 Goteborg, Sweden*

OBJECTIVE: The objective of the research project is to study the relation between different factors in the general and working environment and the presence of cancer in exposed populations. Attempts will be made to relate individual factors as well as environmental exposures to the development of a particular tumor form.

APPROACH: The Swedish National Mortality Registry and the Swedish Cancer Registry are used in the study. With the aid of recorded deaths or registered cases of cancer, the geographical distribution in the country is studied. At sites where accumulations are found, case-related studies are performed to evaluate environmental factors. Studies are also made in specific counties where an increase in the incidence of a particular tumor form has been suspected or in communities where the presence of local industries has been related to the presence of specific tumors, either in the working population or in the general environment.

PROGRESS: An observed increase in the incidence of liver cancer was found to be related to an increase in autopsy frequency. A higher incidence was found in large cities in Sweden, which could be related to alcohol habits, also demonstrating themselves as an increase in the cases of liver cirrhosis.

In a Swedish county a population density gradient was found for lung cancer. As air pollution levels are low, the difference was attributed to differences in smoking habits between rural and urban areas. The cancer increase in one community was related to the handling of asbestos in an industry.

Continued work on the project involves an analysis of the geographical distribution of pancreas and kidney cancer, followed by a study on cancer in children in the age groups up to 10 years.

329. JAPAN-HAWAII CANCER STUDY

Nomura, A. M., Stemmermann, G. N., Levin, D. M., Mower, H. F., Kamiyama, S., Pollack, E., Murray, J., Masuda, H., Kuakini Medical Center, Dept. of Pathology, *347 N. Kuakini St., Honolulu, Hawaii*, 96817, United States of America

In recent years the Japanese in Hawaii have experienced cancer incidence and mortality rates which are intermediate to the rates of indigenous Japanese and US-Whites. Because genetic variables are presumably held constant in comparisons between native and migrated Japanese, this shift in the cancer experience of the 'Westernized' Japanese in Hawaii strongly suggests that environmental factors play a major role in oncogenesis. Furthermore, this spontaneous sociomedical experience among the Japanese provides a unique opportunity to isolate specific environmental, biochemical and pathologic variables which may be etiologically associated with different types of cancerous lesions. Of special interest is the observed reciprocal relationship of gastric and colorectal cancer among the migrant Hawaii Japanese. They have manifested a falling rate for gastric cancer and a rising trend for malignant colorectal tumors. The study has utilized the examined population of the Honolulu Heart Program, which consisted of 8,006 men of Japanese ancestry who were born from 1900 through 1919 and seen from 1965 to 1968 in Hawaii. Approximately 6,800 of the men have since returned for a repeat examination, and these are the men now under surveillance in the Japan-Hawaii cancer study. There are three major end points in this surveillance: (1) The occurrence of new cases of cancer; (2) deaths due to different types of cancer; (3) appropriate pathologic findings from surgical specimens or necropsies.

330. RELATIONSHIP BETWEEN CANCER MORTALITY AND ENVIRONMENTAL FACTORS

Preuss, P. W., Riggan, B., State Dept. of Environmental Protection, *P.O. Box 1390, Trenton, New Jersey*, 08625, United States of America

The proposed project will correlate the geographical patterns of cancer mortality with environmental and industrial data in the following manner: (1) Statewide environmental and industrial data will be collected for as far back in time as the sources permit. (2) A list of approximately 600 environmental and industrial variables will be identified to be correlates to the cancer mortality data. (3) These variables will be correlated to the cancer mortality data. The mathematical techniques will include bivariate correlation and factor analysis. Bivariate correlation is a statistical tool for measuring the relationship between two variables. Factor analysis provides a measure of the extent to which groups of different variables correlated. Through the use of these techniques, both individual factors and groups of factors which correlated with cancer mortality will be identified. (4) From these results of the correlation of the 600 variables, a list of those 20 to 40 which correlate most strongly with cancer mortality will be generated. (5) Intensive data searches will be conducted in order to reconstruct a 30 year period of population exposure to the 20 to 40 selected variables. (6) Annual exposure rates will then be correlated to annual mortality data to determine if relationships exist between exposure and mortality. In performing these correlations the 20-30 year latency period for cancer will be considered. (7) A final report will be prepared explaining all findings and recommending future courses of action.

331. LONG-TERM CANCER MORTALITY TRENDS AMONG KRAKOW INHABITANTS IN RELATION TO DEMOGRAPHY AND ENVIRONMENT

Jedrychowski, W., Cholewka Cabaj, K., Akademia Medyczna W Krakowie, Inst. of Social Medicine, Dept. of Epidemiology, *Ul. Kopernika 7, 31034 Cracow, Poland*

The spatial analysis of mortality due to malignant neoplasms in the population of Cracow will cover the ten-year period 1974-1984. The city of Cracow has over half a million inhabitants and its four districts differ in regard to degree of air pollution, smoking habits, fertility and other social and environmental factors. The aim of the study is to make a comparison between data on mortality from malignant neoplasms in the four districts. Death certificates taken from the statistical office on a monthly basis have been used in the analysis of malignant neoplasms. Cancer mortality data are analyzed according to sex, place of residence and primary site. Age-specific and age-adjusted rates are computed for the total population and for each district. So far, data covering the years 1974-1978 have been collected and are currently being analyzed. The pilot study done for the year 1974 has shown that the most frequent causes of death in Cracow by sex were lung carcinoma in men and breast carcinoma in women. The highest age-adjusted rates were in the city center where the fertility rate was low and the level of atmospheric pollution, tobacco consumption and the proportion of working-class population appeared to be high.

332. MORTALITY, INCIDENCE AND PREVALENCE AS INDICATORS OF THE MAGNITUDE OF THE CANCER PROBLEM WITHIN AN ITALIAN REGION

Mastrandrea, V., Cresci, A. L., Pannelli, F., La Rosa, F., Universita degli Studi di Camerino, Inst. of Hygiene, *62032 Camerino, Italy*

Within the Marche region, located in Central Italy, as within most of the country, there is heterogeneity as far as demographic, socio-economic and environmental characteristics are concerned. Taking into account these considerations, the geography of Marche and the findings of a previous study, an investigation will be carried out for the period 1971 to 1981 into the distribution of mortality, incidence and prevalence by individual tumor sites in the coastal, hill and mountain zones of this

region which can be respectively considered urban, semi-urban and rural. The three zones may represent an ideal compromise between the need for units small enough to be homogenous for demographic and environmental characteristics that might influence cancer risk and yet large enough to provide stable estimates. Mortality, incidence and prevalence data are abstracted from death certificates from the 246 municipalities of the Marche region and from the clinical record cards available in the 90 hospitals of the same region.

333. NATIONAL CANCER INSTITUTE PROGRAM OF CANCER SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS (SEER PROGRAM)

Young, J. L., Austin, D. F., Krementz, E. T., Thompson, D., Piette, L., Key, C. R., Smart, C. R., Honeyman, M., Isaacson, P., Brennan, M. J., Martinez, I., Child, M. A., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst., Biometry Branch, *9000 Rockville Pike, Bethesda, Maryland*, 20205, United States of America

The SEER Program was developed in response to the National Cancer Program requirements for assessing as currently as possible the magnitude of the cancer problem in the United States and for identifying factors related to cancer risk and/or patient survival. The 'cancer problem' has been interpreted to include: 1) newly diagnosed cancer cases that might have been prevented by altering host or environmental conditions and 2) deaths due to cancer that might have been prevented by earlier cancer diagnosis coupled with optimal therapeutic approaches. Therefore, the SEER Program has among its objectives: 1) To assemble and report on a periodic basis, estimates of cancer incidence in the United States. 2) To monitor annual cancer incidence to identify unusual changes in specific forms of cancer occurring in groups defined by parameters of geographical, demographic and social characteristics of the population. 3) To provide continuing information on changes over time in extent of disease at diagnosis, trends in therapy and associated changes in cancer patient survival. 4) To promote the development of hypotheses and specific studies designed to identify cancer aetiological factors (environmental/occupational, sociocultural, etc.) and factors related to patient survival.

334. WISCONSIN CANCER REPORTING SYSTEM - CANCER SURVEILLANCE AND RESEARCH

Woodbury, M. A., Rusch, H. P., State Bureau of Prevention, Section of Epidemiological Surveillance & Assessment, *P.O. Box 309, Madison, Wisconsin*, 53701, United States of America

The overall objective of the epidemiological study section of the Wisconsin Cancer Reporting System is the identification of high risk population groups, environmental factors and potential carcinogenic agents. This is a long-range plan currently directed toward developing the tools necessary for providing a mechanism for identifying cancer morbidity and mortality events or patterns significantly deviating from past trends. A computer program will be written to indicate such occurrences. Specific epidemiological studies will determine the factors involved, should the unusual event or pattern not be the result of changes in reporting habits. A computer program will also be developed to correlate an ongoing basis on various environmental conditions with cancer morbidity and mortality. (For example, a study of the degree of correlation of cancer mortality by distance from a taconite mine with measurements of asbestos in air, water and soil by distance from the mine.) It is anticipated that such computerized surveillance will substantially increase the ability to recognize changes early and to set in action the analytical epidemiological studies required.

335. ENVIRONMENTAL CARCINOGENS AND HUMAN CANCER

Ward, J. R., Nagda, N. L., Geomet Inc., Environmental Health Division, *15 Firstfield Rd., Gaithersburg, Maryland*, 20760, United States of America

This project is part of a US Environmental Protection Agency program investigating the relationship between environmental carcinogens and risk of cancer in the general population. Much of the work to this point has concerned problem definition, methodology and data base development. The program is now focussing on geographical areas that can serve as community laboratories for research on environmental levels of specific carcinogens and their association with cancer risk. An area centered in south-eastern Ohio has been selected for this purpose after screening over 3,000 US counties for coincidence of high cancer mortality and probable exposure. Preliminary investigations to establish the utility of the study area have been completed. The potential for long-term carcinogen exposure has been confirmed through emission source inventory and analysis of available monitoring data. Intra-area mortality analysis has shown significant differences in respiratory cancer associated with proximity to major emission sources. Results from a small case-control study suggest that the increased risk in these source sectors may be related to long-term residence and smoking, but it does not appear to be due to smoking alone or to occupational exposure. Based on this preliminary work the Agency is proceeding with monitoring of carcinogen levels in air, water, soil, flora and fauna, and planning further epidemiological studies.

336. MONITORING FOR CANCER RISKS

Berg, J. W., Ferguson, S. W., Franz, L. W., Silverberg, S. G., Colorado Regional Cancer Center Inc., Division of Epidemiology & Statistics, *1655 Lafayette St., Suite 301, Denver, Colorado*, 80218, United States of America

The ultimate objective is to identify environmental causes producing new increases in cancer risk among residents of the area served by the Colorado Regional Cancer Center. The focus will be on increases of previously rare cancers since large relative increases should be visible even with only early (i.e., incomplete) case ascertainment. A computer program will be created to analyze the monthly updated tape file of the Colorado Central Cancer Registry for increases in cancers of unusual histology or in patient groups in which the cancers had been uncommon. Entities showing a suspicious increase will be selected for two kinds of interview investigation: follow-back on cases already in the Registry files and interviews of new patients as they are admitted to regional hospitals.

337. CANCER DEATH PATTERNS AND THEIR RELATION TO ENVIRONMENTAL FACTORS

Nakachi, K., Kubo, T., Saitama Cancer Center, Dept. of Epidemiology, *818 Komuro, Ina-Machi, Kitaadachi-Gun, Saitama-Ken 362, Japan*

OBJECTIVE: To find some basic patterns in the geographical distribution of cancer deaths, and thus to ascertain what environmental factors relate to those patterns.

APPROACH: A statistical analysis, so-called Principal Component Analysis, is applied to the geographical distribution of cancer standardized mortality ratios, and the basic cancer death patterns thus obtained are examined in relation to various environmental factors.

PROGRESS: The basic patterns of cancer deaths in Saitama prefecture, Japan have been found and analyzed as follows: (1) The most basic patterns for males and females are very similar to each other, and this pattern is shown to be characteristic of residents of Saitama. (2) The second pattern is closely related to the rural or riverside environment although this pattern for males is different from that for females.

338. GEOGRAPHICAL VARIATIONS AND TIME TRENDS OF CANCER MORTALITY IN JAPAN

Kuroishi, T., Tominaga, S., Shimizu, H., Aoki, K., Ogawa, H., Aichi Cancer Center Research Inst., Division of Epidemiology, *81 1159 Kanokoden Tashiro-cho, Chikusa-ku, Nagoya 464, Aichi, Japan*

Mortality from some malignant neoplasms in Japan shows marked variations in geographical distribution and secular trends. This study aims to describe mortality from cancers of 18 sites for each prefecture and smaller administrative districts in Japan (1969-1976) and to find possible cancer risk factors by examining geographical and chronological relationships between mortality from cancers of various sites and various environmental factors, such as air pollution, food intake, smoking, socioeconomic factors, etc.

339. EPIDEMIOLOGICAL STUDIES OF CANCER IN LOUISIANA

Gottlieb, M. S., Pickle, L., Blot, W. J., Tulane University of Louisiana, School of Medicine, Dept. of Medicine, *1430 Tulane Ave., New Orleans, Louisiana*, 70112, United States of America

Death certificates for cancer of the lung, nasopharynx, pancreas and bladder will be identified for selected Louisiana parishes for the years 1960-1975. Controls will be matched by parish of residence, year of death, age (within 2 years), sex and race. The frequency of occurrence of names attributable to groups with a common heritage will also be compared, as will relationship of residence at death and distance from selected industries, and water source. The objective is to determine single or multiple factors which can be identified as associated with a greater risk in cases compared with controls. This will form the basis of subsequent additional observational studies. Sub-studies on populations exposed to unique substances are included.

340. ECOLOGICAL ANALYSIS OF CANCER MORTALITY IN LOWER SAXONY

Pflanz, M., Wolf, E. N., Medizinische Hochschule Hannover, Institut fuer Epidemiologie und Sozialmedizin, *Karl Wiechert Allee 9, D3000 Hannover 61, Federal Republic of Germany*

The study aims to detect relationships between cancer mortality (1968 and 1971) and socioeconomic or environmental factors by multivariate analysis. The sex-specific age-standardized data will be correlated with about 70 socioeconomic variables. Spatial relationship between chemical plants, lead smelters and other environmental hazards on one hand, and counties with high cancer mortality for specific sites on the other hand, will be examined. The study method is similar to that used in the analysis of cancer mortality in the United States counties.

341. GEOGRAPHICAL DISTRIBUTION OF CANCER MORTALITY IN IRELAND

Kevany, J. P., Kaliszer, M., Doherty, M., Allwright, S. P., University of Dublin Trinity College, Dept. of Social Medicine, *Dublin, Ireland*

To determine the spatial distribution of cancer mortality in the population 35 years of age and older and to correlate cancer mortality with natural and man-made environmental variables, standardized mortality rates for each sex and for major cancer categories are computed annually on a continuous basis. Five-year mean frequencies are calculated for each county and subsequently for electoral divisions and for topographical grid units of ten sq.km. Geochemical, soil and water data will be compared with cancer frequencies on the basis of correlation and regression analysis.

342. ENVIRONMENTAL AND OCCUPATIONAL FACTORS AND DISTRIBUTION OF LUNG CANCER AND BRONCHITIS IN UMBRIA

Candeli, A., Mastrandrea, V., Vitali, R. R., Toccaceli, S., Universita degli Studi di Perugia, Faculty of Science, Institute of Hygiene, *via del Giochetto, Perugia, Italy*

Umbria is one of the central regions of Italy. Some areas of this region are very different from others with respect to economic and social development, kinds of industries, density of population and climate. These differences are especially marked between the two biggest cities of the region, Perugia and Terni. Preliminary studies have shown that mortality from lung cancer and from bronchitis is higher in Terni than in Perugia. Research is in progress on atmospheric pollution in these towns which seems higher in Terni than in Perugia. For this reason it is proposed to study retrospectively the mortality and the morbidity from lung cancer and bronchitis in the two cities in relation to environment and occupation.

343. ENVIRONMENTAL ANTECEDENTS OF CANCER

Sterling, T. D., Weinkam, J. C., Kobayashi, D., Simon Fraser University, School of Interdisciplinary Studies, *Burnaby, British Columbia, Canada*

An attempt is being made to determine the relative effects on cancer of various sources of pollution - from occupation, from community sources, and from tobacco products. Analysis is based on a number of data files that have been collected concerning mortality of the U.S. veterans' population (previous Dorn Study), on the 1969 through 1974 survey results of the Household Interview Survey of the National Center for Health Statistics, on files on Occupational Compensation claims, and from direct studies of a population of workers in a pulp and paper mill on Vancouver Island.

344. ENVIRONMENTAL AND OCCUPATIONAL CANCER MORTALITY ESTIMATION

Symons, M. J., Dement, J. M., University of North Carolina, Chapel Hill Campus, School of Public Health, Dept. of Biostatistics, *Rosenau Hall, 201H, Chapel Hill, North Carolina*, 27514, United States of America

Environmental contributions to cancer mortality will be estimated based on a proposed model using age-specific cancer death rates by cancer site. Background age-specific cancer rates by site will be estimated using NCI data on cancer mortality among U.S. counties. Various methods for estimating these background rates will be explored.

Occupational cancer mortality will be estimated by comparing U.S. death rates for white males and white females. Various adjustments will be compared for sex-linked cancers and different smoking patterns.

345. ETIOLOGIC STUDIES OF CANCER IN NEW JERSEY

Altman, R., State Dept. of Health, *John Fitch Plaza, P.O. Box 1540, Trenton, New Jersey*, 08625, United States of America

OBJECTIVES: Expand the retrospective studies to include cancers other than bladder such as colon, rectum, breast, and lung cancers. Continue analyses of industrial and environmental variables (water supplies, air polution indices, etc.). Pursue methodologies to develop and test hypotheses concerning relationships between occupational and environmental variables and malignancy. Provide information on descriptive epidemiology of common cancer types in New Jersey.

346. ENVIRONMENTAL CORRELATIONS OF CANCER MORTALITY

Bouckaert, A., Universite Catholique de Louvain, Ecole de Sante Publique, Service d'Epidemiologie, *Clos Chapelle aux Champs 30, 1200 Brussels, Belgium*

Cancer mortality data are correlated with environmental (temperature, sunshine, rainfall, pollution, hardness of water) data. Changes are correlated with changes in the environment.

347. ETIOLOGY OF CANCER

Doll, R., Wald, N., Peto, J. A., Kinlen, L. J., Cook, P. J., Peto, R. G., University of Oxford, Dept. of Social & Community Medicine, *S. Parks Rd., Oxford OX2 6HE, England, United Kingdom*

Environmental and hereditary causes of cancers of different organs; effects of smoking, ionizing radiations, diet, drugs, cosmetics, infections, immunological defects, and occupation.

IV. DETECTION AND MEASUREMENT OF ENVIRONMENTAL AND OCCUPATIONAL CARCINOGENS

A. SAMPLING AND ANALYTICAL TECHNIQUES

348. TRACE ANALYSIS OF AQUEOUS CHLORAMINES

Gray, E. T., University of Hartford, School of Arts & Sciences, Dept. of Chemistry, *200 Bloomfield Ave., West Hartford, Connecticut*, 06117, United States of America

Chloramines in the environment are primarily formed as a result of the chlorination of potable and nonpotable waters. The destruction of harmful bacteria, which is the main purpose of chlorination, is certainly beneficial, but the chloramines which remain as residue from the process are extremely toxic to aquatic life. Interaction of chloramines and macrophage has recently been implicated in terms of cancer. Further effects of chlorine and chloramines on humans at low levels are virtually unknown.

The control of aquatic 'kills' and investigations of the effects of chloramines on humans cannot presently be accomplished as they would require the ability to measure the presence of chloramines in the micromolar-nanomolar range. This is currently not possible in an analytical manner. Historically, chloramine chemistry has been observed to be generally irreproducible, hence the lack of the development of sensitive analytical methods. We have succeeded in analyzing the cause of this generally reported irreproducibility and are able to prepare remarkably stable chloramine solutions which exhibit reproducible behavior. We are, thus, in a unique position to develop sensitive analytical procedures to detect and quantitatively analyze aque-

ous chroramines in ultratrace concentrations. This will be done by first understanding the electron transport properties of chloramines and then applying these properties in the development of measurement systems involving fluorescence and/or chemiluminescence. These two techniques are readily sensitive in the micromolar-nanomolar range. These two techniques offer a further advantage in that once the methods are developed, they have the potential of being implemented using inexpensive and uncomplicated equipment, most of which would already be present in a water chemistry laboratory.

349. TOXIC COMPOUNDS FORMED BY THE CHLORINATION OF ARIZONA SURFACE WATERS

Steelink, C., University of Arizona, School of Liberal Arts, Dept. of Chemistry, *Tucson, Arizona*, 85721, United States of America

Chlorination of drinking water may produce chloroform and other halocarbons. Many of the compounds are toxic and carcinogenic. They arise from the interaction of certain classes of dissolved organic matter and chlorine.

In Arizona, the extent of severity of this reaction is unknown. The purpose of this proposal is threefold: (1) To determine the amount of chloroform and other haloforms produced by chlorination of typical water samples from the major domestic water supplies in Arizona, (2) to analyze the extracts of the leaves and bark of the dominant flora in the principal watersheds in Arizona, (3) to examine the chlorination reaction itself in order to determine those conditions (pH, chlorine concentration, temperature, light) which control the production of toxic compounds.

This information is vital for water quality managers who must assess the potential hazards of chlorination and devise suitable means to reduce these hazards and conform to the newly established guidelines of the Environmental Protection Agency.

350. DETERMINATION OF MUTAGENIC CARBOLINES FORMED ON PYROLYSIS OF FOSSIL FUELS AND A STUDY OF THEIR BIOLOGICAL EFFECTS

Shaw, E. N., Lacks, S., U.S. Dept. of Energy, Brookhaven National Lab., Dept. of Biology, *Upton, New York*, 11973, United States of America

A new class of mutagens and carcinogens has recently been detected in Japan that originates from the pyrolysis of proteins and is found in charred food products and in smoke. The active materials are different from the currently studied polycyclic hydrocarbons since they contain nitrogen. One group of materials arises from the tryptophane of protein and consists of two classes of carbolines: Type A - mutagenic and carcinogenic; and Type B - non-mutagenic but comutagenic (that is, enhances the mutagenic activity of other mutagens). The presence of additional active, nitrogen-containing materials is indicated by preliminary work. Since fossil fuels are derived from organic material, the presence of these mutagens and carcinogens represents a potential health hazard associated with coal technology that must be evaluated. In particular, these materials may be the basis for the observation that the mutagenicity of unfractionated smoke or tar is considerably greater than can be accounted for by the content of benzpyrene alone. In addition, new waste technology involving the combustion of garbage as a conservation effort may also result in the release of carbolines as by-product pollutants. The proposed work seeks to provide a method for the determination of carbolines and related nitrogenous products of combustion in several chromatographic systems. Isolated pure carbolines will be assayed for mutagenic and comutagenic activity in the expectation that more detailed information on the health effects due to fossil fuel combustion will be obtained.

351. ENVIRONMENTAL BLADDER CARCINOGENS

Radomski, J. L., Poupko, J. M., Hearn, W. L., University of Miami, School of Medicine, Dept. of Pharmacology, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida*, 33152, United States of America

The main objectives of the project are to search for unrecognized bladder carcinogens in the human environment and to understand the mechanism of cancer induction by the aromatic amines. Drugs, food additives, and industrial compounds are being considered. The metabolism of suspect chemical will be examined in urine and by in vitro incubation with bladder microsomes, to determine whether carcinogenic N-hydroxy metabolites are formed. Bovine bladder microsomes have been shown to be especially active in N-hydroxylating carcinogenic aromatic amines.

Gas chromatography utilizing the electron capture detector, HPLC and GC-mass spectrometry will be the primary analytical methods used. Compounds being studied include caffeine, theobromine, theophylline, sulfadiazine, p-aminosalicylic acid, ampicillin, phenacetin, acetaminophen and acetanilid. Industrial amines being evaluated in dogs are methylenedianiline, 4,4'-methylene-bis (2-chloroaniline), dichlorobenzidine, 2,2-bis(p-amino-phenyl) propane and 4,4'-methylene-bis-(2-methylaniline). The N-hydroxy and nitroso derivatives of these amines are being synthesized.

Previous results show that dimethylnitrosamine is formed in the bladder during urinary tract infection. If DMN is an etiological factor in bladder cancer, it must be shown that it can be activated by and react with bladder mucosa. Examination of bladder mucosa has shown the presence of cytochrome P-450 which is capable of type II binding. These microsomes are capable of N-hydroxylating 4-aminobiphenyl. Possible activation of DMN is still under investigation.

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352. ION CHROMATOGRAPHY ANALYSIS OF AROMATIC AMINES

Frohliger, H., University of Pittsburgh, School of Arts & Sciences, Dept. of Chemistry, *4200 5th Ave., Pittsburgh, Pennsylvania*, 15260, United States of America

OBJECTIVE: The objective of this research project is to develop a liquid chromatographic method for the separation and analysis of amines found in environmental samples. The liquid chromatographic method to be utilized is a modification of ion chromatography as described by H. Small, T.S. Stevens and W.C. Bauman, 'Novel Ion Exchange Chromatographic Method Using Conductimetric Detection,' Anal. Chem. 47, 1801 (1975). The amines to be examined are aromatic amines, many of which are known or suspected carcinogens. The environmental samples to be utilized will be obtained on Hi-Volume filters. These filters will be collected in the vicinity of sources of amines such as coke works and dye manufacturing facilities. Emissions from these types of sources have been implicated in lung and bladder cancers.

FINAL OUTPUT: Method for the analysis of aromatic amines.

PROGRESS: Grantee is also investigating benzidine compounds.

353. MOVEMENT, PERSISTENCE AND CONCENTRATION OF PESTICIDES IN SOILS AND AQUATIC ENVIRONMENT

Nash, R. G., Helling, C. S., Isensee, A. R., U.S. Dept. of Agriculture, Agricultural Research, Agricultural Environmental Quality Inst., Pesticide Degradation Lab., *Bldg. 050, Room 100, Beltsville, Maryland*, 20705, United States of America

OBJECTIVE: Develop methods to study the vertical movement adsorption and persistence of pesticides in soils. Measure the distribution, persistence and bioconcentration of pesticides in aquatic food chains.

APPROACH: Conduct comprehensive studies on the downward movement of pesticides by the use of soil thin layer chromatography, the adsorption of organic pesticides by various soil fractions and the persistence of pesticides in soils by chemical and bioassay techniques. Determine the distribution, persistence and bioconcentration of C-labeled pesticide in a microecosystem composed of soil, water, daphnia, snails, and fish.

PROGRESS: Two computer programs were developed for (1) analyzing pesticide interactions when two pesticides indicate phytotoxic synergism or antagonism and (2) a bank of abstracted information and calculated rates of chemical dissipation in soil, plant, water, and air. Batch adsorption coefficients

were measured for eight organic chemicals in soils, as part of an overall program to evaluate adsorption protocols and elucidate chemical structural parameters that affect adsorption. The dialkyl phthalates DBP and DEHP were almost completely adsorbed. For six other organics, the relative order of decreasing adsorptivity, in a sterile soil, was toluene, benzene, aniline, phenol, benzoic acid, and isobutyric acid. Procedural recommendations from these studies include elimination of headspace (when using volatile chemicals) and using sterilized soil (when chemicals are easily biodegraded). The fate of 3,4-dichloroaniline (DCA) (a major metabolite of the herbicide propanil) in submerged soil, rice plants, water, and aquatic organisms was determined using rice paddy microecosystems. Recovery of DCA and metabolites of DCA were similar to results from nonmicroecosystem studies. A maximum of 4.2% of the DCA applied to soil moved into water where it was rapidly degraded and only small amounts of DCA were taken up by aquatic organisms.

354. COAL-OIL MIXTURES TOXICOLOGY

Raabe, C., University of California, Davis Campus, Graduate School, *Davis, California*, 95616, United States of America

This research addresses the problems associated with potentially toxic emissions which are associated with various stages of coal conversion processing for the production of synthetic oil or gas, with emphasis upon the potentially carcinogenic polynuclear aromatic hydrocarbons. Although there are no near full-scale demonstration plants now producing synthetic oil or gas, coal tar volatiles similar to those expected in coal conversion are present in coke ovens currently in use in various industries. These studies address the physical and chemical characterization and biological testing of emissions from a representative coke oven system at a steel mill in the western U.S. These results will contribute directly to planned coal conversion systems with respect to extending our understanding of the toxic species in potential fugitive emissions. Chemical characterization will be done on the basis of aerodynamic size distribution to identify the specific species associated with the respirable fraction of released and condensed hydrocarbons which in the past have been epidemiologically related to the high incidence of lung, bronchial and tracheal cancer as well as cancer of digestive organs and peritoneum in coke oven-workers. Following physical and chemical characterization, a system will be developed to generate surrogate aerosols for use in laboratory studies designed to identify and evaluate the relative importance of selected chemical species. Biological exposure studies will proceed in parallel to the characterization studies. This will be begun with field collected samples and isolated hydrocarbon fractions. Biological testing will include inhalation, ingestion and dermal exposures of small rodents. Since combinations of inorganic particles and polynuclear aromatic hydrocarbons have been reported to be more toxic than these agents individually, we will also study particle-carcinogen synergisms.

355. POLYCYCLIC AROMATIC HYDROCARBONS IN THE ENVIRONMENT

Harkin, J. M., University of Wisconsin, Madison Campus, Agricultural Experiment Station, Dept. of Soil Science, *116 Agricultural Hall, Madison, Wisconsin*, 53706, United States of America

OBJECTIVES: Determine the distribution and levels of polycyclic aromatic hydrocarbons in soil, water and plants in relation to point or diffuse sources of origin, e.g. from power plants, incinerators, oil refineries, and automobile or marine engine exhausts. Make recommendations for land or water use that will avoid health hazards due to elevated concentrations of carcinogenic or cocarcinogenic polynuclear aromatic hydrocarbons.

APPROACH: Samples of soils, water, and plant materials will be collected from areas where enrichment of polycyclic aromatic hydrocarbons might be expected, e.g. from fallout near incinerators or oil refineries, from automobile exhausts near highways and in metropolitan areas, or from marine engine exhausts near marinas, as well as from control areas where background levels can be established. The hydrocarbon mixtures will be extracted, separated by high-pressure liquid chromatography and/or gas chromatography, and assayed by fluorescence spectroscopy. Regions of enrichment of these hazardous chemicals will be identified. Recommendations for land and water use in these areas will be made which will minimize the health hazard for these compounds.

PROGRESS: The methodology for the isolation of polycyclic aromatic hydrocarbons (PAHs) from soils and their analysis has been further improved: Air-dry soil samples are Soxhlet continuously extracted with purified benzene. The extracts are concentrated and filtered through Millipore teflon filters to remove suspended particulates; alkaline permanganate oxidation is used to convert the interfering organic matter to easily separated compounds; preparative thin-layer chromatography on silica gel using cyclohexane/carbon tetrachloride (19/1) separates the PAHs from more polar organics; PAHs are extracted with dichloromethane and concentrated to 1 ml for analysis by gas chromatography. The analysis is qualitative and quantitative for PAHs with 4 through 6 condensed rings. PAH levels in various soils have been compared. Analysis has shown that PAH levels are closely related to the organic matter content of the soil. PAH levels decrease sharply with depth in the soil profile. Rural areas have lower PAH levels than urban areas. Correlation of human activity and PAH levels is not yet possible, because there is still insufficient data. (Text Abridged.)

356. POLYCYCLIC AROMATIC HYDROCARBON POLLUTION IN WATER SYSTEMS

Smith, S. R., Tanaka, J., Collins, R., Johnson, J., University of Connecticut, Storrs Campus, Graduate School, Dept. of Chemistry, *Storrs, Connecticut*, 06268, United States of America

The proposed research includes laboratory and field investigations to (1) develop analytic methods for the determination of polycyclic aromatic hydrocarbons in water supply systems, watersheds and sewage systems, (2) study the extent of this form of pollution in Connecticut water systems, (3) determine the extent of adsorption of polycyclic aromatic hycrocarbons on soils to determine the extent of pollution of drainage areas and sludges and the removal of these potentially hazardous carcinogens from water systems.

The analytical approach will include concentration of the samples by adsorption on polymeric materials, solvent extraction and cryogenic concentration. Identification will be carried out by gas, liquid and thin layer chromatography in conjunction with mass spectrometry and NMR.

357. RADIOECOLOGY OF URANIUM AND RADIUM WITH SPECIAL REFERENCE TO A URANIUM MINING AREA

Stegnar, P., Kosta, L., Byrne, A. R., Ravnik, V., Kobal, I., Univerza v Ljubljani, Josef Stefan Inst., Nuclear Chemistry Section, *Jamova 39, 61001 Ljubljana, Yugoslavia*

The general aim is to follow the concentrations and distribution of U and Ra-226 at different trophic levels of the human food chain according to the present and future nuclear acitvities from the uranium mining area. Subsequently, studies on the absorption of U and Ra-226 and their transportation through representatives of possible indicator organisms will be made.

In the present study a radiochemical neutron activation method is being used for the determination of trace amounts of U in the environmental samples, and the alpha-scintillation technique for radium analyses.

Techniques for the preparation of biological samples will be also developed in order to allow reliable interpretation of the results obtained.

358. PIXE ANALYSIS OF HAIR SAMPLES FOR TRACE ELEMENT CONTAMINATION

Baptista, G. B., Paschoa, A. S., Montenegro, E. C., Pontificia Universidade Catolica do Rio de Janeiro, Dept. of Physics, *Rua Marq. de Sao Vinc. 225, Gavea Caixa Postal 38071, Rio de Janeiro 22453, Brazil*

We are currently analyzing in our laboratory one hundred hair samples to detect chromium contamination of the population of a Mexican city.

The target is prepared by mounting on an aluminum frame of up to eight strands of hair. As the hair can be considered a thick target for irradiation with 2 MeV protons, problems may arise in the analysis of data due to: loss of energy of incident particle with penetration depth, X-ray self-absorption and lack of knowledge of elemental distribution in the hair. We have discussed these problems and derived expression to estimate the uncertainty in the analysis due to the effects mentioned above.

This discussion permits to establish the experimental conditions for a meaningful analysis of hair strands.

359. ASBESTOS AND CANCER

Warnock, M. L., Churg, A. M., University of California, San Francisco Campus, School of Medicine, Dept. of Pathology, *551 Parnassus Ave., San Francisco, California*, 94122, United States of America

Our previous studies have failed to demonstrate a relation between numbers of pulmonary asbestos bodies and the presence of carcinoma of the lung or gastrointestinal tract in workers with very low asbestos exposure. Asbestos bodies, however, represent only a part, and perhaps only a small part, of the total lung asbestos burden, which is composed of coated bodies as well as uncoated fibers. It remains possible that a relation exists between numbers of uncoated asbestos fibers and the presence of bronchogenic carcinoma. This study will attempt to quantify and type the uncoated asbestos fibers as well as asbestos bodies at various sites in the lung. A new preparative method has already been developed and used for examining and identifying the nature of the cores of asbestos bodies by electron diffraction. The same method will be used to identify further these same bodies by electron micropore analysis. An additional preparative method has been devised for recovering uncoated asbestos fibers. Relations between numbers of coated and uncoated asbestos fibers, as well as their relative locations within the lung, will be tabulated, and an attempt will be made to correlate numbers or types of fibers with the presence or absence of carcinomas. We have previously shown that numbers of asbestos bodies are related to occupation and an attempt will be made to establish whether a similar situation exists for uncoated fibers or whether they are derived from the environment.

360. MINERAL FIBERS AND LUNG CANCER

Churg, A. M., University of California, San Francisco Campus, School of Medicine, Dept. of Pathology, *551 Parnassus Ave., San Francisco, California*, 94122, United States of America

Epidemiologic studies of lung cancer indicate that there are marked incidence variations which cannot be accounted for by cigarette smoking patterns, but do appear to relate to variables such as race, socioeconomic status, and geographic location. Air pollution is another factor which has sometimes been implicated in lung carcinogenesis, primarily on the basis of urban vs. rural cancer rates. Mineral fibers constitute a portion of the particulate fraction of urban air pollution, and it has been shown in animal studies that, under appropriate conditions, many particulates and especially mineral fibers may be carcinogenic or co-carcinogenic. Mineral fibers are known to be present in large numbers in the lungs of urban dwellers. This research involves an investigation to determine if there is an association between lung burden of fibrous minerals and bronchogenic carcinoma in a general urban population in a geographically high lung cancer area. Numbers of mineral fibers will be quantitated at the light and electron microscopic level by dissolving autopsy and surgical lungs and collecting appropriate samples. Whole lung slices will be used to minimize topographic variation in numbers of fibers. Fibers will be further identified by electron diffraction and electron microprobe to determine mineral species, and will also be enumerated by lengths and diameters; the latter properties appear to be important in carcinogenesis. An attempt will be made to correlate total fibers, fiber specific mineral type, and/or fibers of various size classes with the presence or absence of bronchogenic carcinoma.

361. SRC EFFLUENT/PRODUCT CHARACTERIZATION

Weimer, W. C., U.S. Dept. of Energy, Battelle Pacific Northwest Lab., *P.O. Box 999, Richland, Washington*, 99352, United States of America

The solvent refining of coal is a rapidly developing advanced fossil fuel energy technology. The objective of this research is to assure that all potential environmental and health concerns are evaluated prior to full-scale commercialization of this coal liquefaction process. Samples of SRC-I and SRC-II products, effluents, process streams, and waste materials are being obtained from the Solvent Refined Coal Pilot Plant facility in Du Pont, Washington, and from smaller PDU facilities when such units more closely approximate demonstration plant or commercial plant operating conditions. These materials are chemically characterized, fractionated, and prepared for biological and/or ecological testing. Additional chemical characterization is being performed to identify the biologically active organic compound classes and individual organic constitutents present. The coordination between the chemical analyses and the biotesting program assures that the most detailed chemical characterization information is obtained for those SRC research materials of greatest biological concern. During FY 1979, we have identified some of the individual compounds in SRC products which are expressing themselves as microbial mutagens in the Ames bioassay procedure. During FY 1980, we will continue to work toward the identification of all of the SRC constituents that behave as mutagens and will work closely with process engineers in evaluating the process conditions which will reduce the concentrations of these mutagens in the final SRC products.

362. OIL SHALE AND TAR SAND EFFLUENT CHARACTERIZATION

Fruchter, J. S., U.S. Dept. of Energy, Battelle Pacific Northwest Lab., *P.O. Box 999, Richland, Washington*, 99352, United States of America

This study will identify potential pollutants which may reach the environment as a result of emissions from oil shale and tar sand retorting operations. Such a study is necessary at the present time because of current vigorous interest in oil shale and tar sand technology being shown by both private and government sectors. Effluents from both above-ground and in situ processes will be characterized for a wide spectrum of inorganic, metallorganic and organic compounds and species. A wide variety of analytical methods, including gas chromatography-mass spectroscopy, neutron activation, x-ray fluorescence, high pressure liquid chromatography, atomic absorption and plasma DC-emission spectroscopy, will be used for the characterization measurements. Effluents to be characterized will include raw oil shale, spent shale, crude shale oil, various shale oil boiling fractions, upgraded shale oil, process water, off-gases, as well as tar sand and crude oil from the sand. Priority will be given to those processes which show promise of early commercialization. On analysis, priority will be given to compounds of elements known or suspected as being carcinogenic, toxic or otherwise harmful. A list of such compounds and elements to be looked for will be formulated and reported as part of the project. Source term calculations will be made for each process.

363. SURVEY OF THE PREVALENCE OF FERRUGINOUS BODY (ZEOLITE) IN SPUTUM OF THE INHABITANTS OF KARAIN

Baris, Y. I., Sebastien, P., Hacettepe Universitesi, Faculty of Medicine, Dept. of Chest Diseases, *Ankara, Turkey*

Recent epidemiological work carried out in the village of Karain revealed that malignant mesothelioma and chronic fibrinous pleurisy are endemic. Mineralogical data show that these disorders are probably due to the presence of a fibrous silicate (zeolite) other than asbestos which is found in the tuff rocks in Karain, in the airborne samples and even in the lung tissues of the patients. A survey is planned in order to demonstrate ferruginous bodies (zeolite) in the sputum of the inhabitants of Karain using the neighboring village of Karlik as a control. The level of exposure will be assessed and correlated with cancer rates.

364. ORGANIC POLLUTANTS IN GROUND-RECHARGED WATER

Bohn, H., Steelink, C., University of Arizona, School of Agriculture, Dept. of Soils, Water & Engineering, *Tucson, Arizona*, 85721, United States of America

The organic compounds in the secondary sewage effluent treated and reclaimed by land spreading effluent will be isolated, separated, and identified. Earlier work on this water purification system indicated that the resulting water is perhaps potable. Complete identification of the waterborne organic compounds is necessary before water from this treatment can be used for municipal purposes. Of major concern is the presence of toxins, carcinogens, chelating agents and taste and odor compounds.

Analytically, the first part of this project will be focused on developing a non-destructive sampling technique to isolate the major organic constituents from the recharged water. A number of resin systems and other methods will be evaluated by

laboratory and field studies. The second part will involve the separation and identification of the pollutants. Various types of chromatography, mass spectrometry, nuclear magnetic resonance and infrared spectroscopy, among others, will be employed.

365. IDENTIFICATION OF NONVOLATILE MUTAGENS IN DRINKING WATER AND SURFACE WATER

Johnston, J. B., University of Illinois, Urbana-Champaign Campus, Inst. for Environmental Studies, *408 S. Goodwin, Urbana, Illinois*, 61801, United States of America

OBJECTIVE: The objective of this project is to investigate the potential of an adsorption/distillation scheme for its applicability in isolating organic substances from water. The system will be optimized by varying the types of adsorbents used.

APPROACH: The recovery of 23 selected organic compounds from water containing specified levels of inorganic ions will be determined. Mass balances will be calculated to determine exactly what happens to each compound during the process. The method will be used to isolate organic matter from selected surface and drinking waters. Ultimately nonvolatile organic mutagenic substances will be identified.

366. ANALYTICAL APPLICATIONS OF MASS SPECTROMETRY TO CARCINOGENESIS PROBLEMS

Roller, P. P., Keefer, L. K., Miller, J. R., Weisburger, E. K., Grantham, P. H., Benjamin, T., Slavin, B. W., Sporn, M. B., Frolik, C. A., Gelboin, H. V., Angeles, R. M., DeLuca, L. M., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst., Analytical Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland*, 20205, United States of America

The laboratory is involved in carrying out independent research, as well as participating in collaborative projects on carcinogenesis related problems, where mass spectrometry can be used as an analytical tool to determine the structure or confirm the identity of non-polymeric organic molecules of interest. Studies include: (1) the identification of carcinogen metabolites in activation and metabolism studies; (2) the identification of naturally occurring potential carcinogens in the environment; (3) elucidation of mass spectral fragmentation mechanisms; (4) development of methods for derivitization and analysis of carcinogens; (5) analysis of bioactive materials that may play a role in cancer causation and prevention mechanisms, such as vitamin A derivatives and substances with immunological properties; (6) application of nuclear magnetic resonance spectroscopy to structural problems.

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367. DEVELOP MULTI-RESIDUE ANALYSIS FOR 20 SIGNIFICANT CARCINOGENS AND SCREENING TECHNIQUES FOR ANALYSIS OF CHEMICAL CLASSES (ABBREV)

McMillin, C. R., Monsanto Research Corp., *1515 Nicholas Rd., Box 8, Dayton, Ohio*, 45407, United States of America

OBJECTIVE: Identify 20 of the most significant suspected atmospheric carcinogens that are produced in high volume and develop analytical methodology for their analysis.

APPROACH: Perform a literature survey of the high volume chemicals that are carcinogens or suspected carcinogens. From this survey, 20 chemicals are to be selected for development of methods for their subsequent collection and analysis.

PROGRESS: The twenty compounds have been selected from a compilation of 125 chemicals suspected of being carcinogens. They were selected to be representative of the broadest range of chemicals possible. Methodology for the analysis of these 20 chemicals has been developed and is currently being evaluated. A EPA report on the 1st year's results is available, EPA-600/2-80-015.

368. STUDY OF THE WATER DISTRIBUTION SYSTEM AS A POTENTIAL SOURCE OF MUTAGENS/ CARCINOGENS IN DRINKING WATERS

Saxena, J., Basu, D. K., Schwartz, D. J., Syracuse Research Corp., Center for Chemical Hazard Assessment, *Merrill Ln., Univ. Heights, Syracuse, New York*, 13210, United States of America

OBJECTIVE: The proposed study is concerned with assessing the mutagenic/carcinogenic potential of drinking water reaching the public, and with evaluating the role of the distribution process in contributing these substances. The sampling locations selected for this study represent the largest water supplies within the 18 selected counties in the U.S. The areas these supplies serve represent both high and low cancer incidence areas.

APPROACH: The overall mutagenic/carcinogenic activity shall be determined utilizing bioassay systems, e.g., Ames Salmonella assay. The analysis shall be performed on raw water, on finished water at the treatment plant, and on samples collected from various points in the distribution system representing exposure to different types of distribution pipes and different lengths of pipes. The assay shall be performed on the waters and on the organic fraction recovered from water using polyurethane foam columns. In view of the potential of distribution pipes for addition of polynuclear aromatic hydrocarbons, the presence of these chemicals in various waters shall also be examined.

PROGRESS: Analysis of 9 water supplies completed on schedule. No significant concentrations of polynuclear aromatic hydrocarbons were found.

369. MULTI-MEDIA SAMPLING FOR SELECTED CARCINOGENS

Crockett, A. B., U.S. Environmental Protection Agency, Office of Research & Development, Environmental Monitoring & Systems Lab., *P.O. Box 15027, Las Vegas, Nevada*, 89114, United States of America

OBJECTIVE: To determine environmental levels of various pollutants in areas of high human exposure.

APPROACH: Multi-media samples will be collected and analyzed to determine levels of specific pollutants. The residue levels provide some data on the potential for human exposure.

B. MUTAGENICITY TESTS

370. MUTAGENESIS BY METALS OF ENVIRONMENTAL SIGNIFICANCE

Rossman, T. G., Kneip, T. J., New York University, School of Medicine, Dept. of Environmental Medicine, *100 Washington Sq. E., New York, New York*, 10003, United States of America

Environmental exposure to certain metals has been correlated with increased cancer incidence. Most carcinogens or their metabolites have been shown to be mutagenic. This has not been the case for carcinogenic metals. This proposal seeks to unravel the mechanism of metal mutagenesis and to determine whether some metals might also act as co-mutagens. These studies will involve a comparison of the effects of metals on prokaryotic and eukaryotic systems. Carcinogenic and non-carcinogenic metals will be analyzed in these two systems for toxicity, ability to cause mutations, and ability to interfere with DNA repair or otherwise act as comutagens. It is one of the assumptions of this proposal that existing tester strains of bacteria are inadequate for metal mutagenesis because they have been developed to test mutagenesis by agents which cause bulky lesions on DNA. The process of analyzing the mechanism of metal mutagenesis (which may be fundamentally different from the mechanism of most organic compounds) will involve utilization of E. coli mutants with a variety of DNA repair deficiencies. Some of these mutants should be more sensitive to metal mutagenesis, and could then be added to the existing stock of tester strains to screen for other agents which are mutagenic by mechanisms similar to those of metals.

371. A STUDY OF MUTAGENESIS BY CHEMICAL CARCINOGENS

Cavalieri, L. F., Sloan Kettering Inst. for Cancer Research, *410 E. 68th St., New York, New York*, 10021, United States of America

This proposal is concerned with mutagenesis and carcinogenesis induced by aromatic polycyclic hydrocarbons which are environmental pollutants. The experiments described will show whether, and how, DNA adducts formed from the proximate carcinogens produce mutations. Our study offers a new approach: we will use the mammalian virus SV40, with its DNA modified in vitro by treatment with the proximate hydrocarbon carcinogen. The modified and characterized SV40 DNA vector will then be studied in infected cells from which we will learn the molecular nature (base change, insertion, deletion) and location of mutations caused by the hydrocarbon adducts. Our studies will also help to elucidate the role of DNA repair in mutagenesis. We will study both pre- and post-replicative repair and will determine whether the repair process itself is error-prone. A close correlation between mutagenesis and carcinogenesis will be made possible by examining the extent of mutagenesis of SV40 in the same cells in which transformation by the hydrocarbons will be studied. This last approach will also provide a basis for the screening of potential carcinogens.

372. MUTAGENIC SPECIFICITY OF ENVIRONMENTAL CARCINOGENS

Eisenstadt, E., Haseltine, W. A., Brash, D., Harvard University, Boston Campus, School of Public Health, Dept. of Microbiology, *55 Shattuck St., Boston, Massachusetts*, 02115, United States of America

The basic objective of this research program is to develop specific information about the spectrum of mutations that can be induced by environmental carcinogens. We propose to study, at the nucleotide level, the DNA alterations that are generated by carcinogens in the lacI gene of Escherichia coli. We will determine the mutagenic spectrum induced by ultraviolet light and cyclopenta(cd)pyrene in bacteria with different DNA repair capabilities. The information we expect to obtain from these studies includes: 1) the full range of mutational events that arise from damage to DNA by selected environmental carcinogens: 2) the influence of certain genes governing the enzymatic repair of DNA lesions on the mutagenic spectrum of carcinogens: 3) the effect of primary structure (sequence) on the conversion of DNA lesions to mutations.

To develop this information, we shall induce and map mutations in the lacI gene carried on an F' factor. The mutation will then be crossed onto a plasmid whose copy number can be amplified. The isolated plasmid will be cut with a restriction enzyme to remove the region containing the lacI gene. The 5' ends of this fragment will be labelled with 32p and the labelled DNA will be cut with a set of restriction enzymes to generate fragments that are suitable for sequencing by the Maxam-Gilbert method.

373. COMPARATIVE EFFECT OF IRRADIATION AND METABOLIZATION OF SOME CHEMICAL POLLUANTS IN ANIMALS BASED UPON MUTAGENIC/CARCINOGENIC ACTIVITY

Niculescu Duvaz, I., Voiculetz, N., Sbenghe, M., Barbu, C., Focsaneanu, O., Academia de Stiinte Medicale, Institutul Oncologic, Dept. of Chemical Carcinogenesis, *Bd. 1 Mai No. 11 Sector 1, P.O. Box 1005, 78159 Bucharest, Romania*

The project objectives deal with a study on the mutagenic and carcinogenic potential of some chemical compounds entering man's environment.

For estimating the potential of production consequences of certain chemicals (polycyclic aromatic hydrocarbons, ethylene oxide and their metabolic derivatives) the authors will use the short-term tests (bacterians: mutatest and inductest; biochemicals: repair inhibition, DNA strand separation in alkali by hydroxyapatite chromatography, and the rate of DNA semiconservative synthesis in irradiated or chemical treated rat splenic lymphoid cells).

The performed research should enable a comparison of these chemical-induced biological effects with those caused by low doses of radiation.

Such information bases are indispensable in the assessment of comparative health impacts of nuclear and fossil fuel energy alternatives - a problem confronting all populations and nations.

374. TRITIUM DAMAGE IN MAMMALIAN CELLS

Burki, H. J., University of California, Berkeley Campus, Lawrence Berkeley Lab., *Berkeley, California*, 94720, United States of America

One major objective of these studies is to gain information on the mechanisms which lead to inactivation or the mutagenesis of several types of mammalian cells in vitro. The other major objective is to provide a quantitative framework for evaluating the effects of tritium disintegrations and related types of damaging agents in different parts of the mammalian nucleus, including hot spots for killing and mutagenesis. Using agents like 3H, 14C, 125I, Er, and I incorporated into the DNA of synchronized mammalian cells, the resulting effects on mutations and other experimental endpoints will be related to the time in the life cycle when the effects are important and the position of the DNA where the damage occurs. These results will be compared to results obtained from exposure to random damaging mutagenic agents. Certain genetic studies not yet possible in mammalian cells will be performed using diploid yeast. This information will be useful in constructing conservative estimates of world health effects due to tritium by products associated with fission and proposed fusion power generation.

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375. ALKYLATING-CARCINOGEN MUTAGENESIS IN MAMMALIAN CELLS

Burki, H. J., University of California, Berkeley Campus, Lawrence Berkeley Lab., Donner Laboratory, *Berkeley, California*, 94720, United States of America

It is proposed to develop a model system for studying the mutagenesis of alkylating carcinogens in asynchronous and synchronous mammalian cells in vitro. Using asynchronous cells of different species and tissue origin, we will measure the production of mutations by ethylnitrosourea (ENU) and related environmental carcinogens. We will determine the effects of cellular repair processes on the induction of mutations by measuring the loss of carcinogen-produced damage and relating it to mutagenesis. In addition, we will measure the induced frequency of certain specific mutations during the cell cycle to test if specific mutagenic changes are associated with specific cell-cycle times.

ENU is used because of its advantageous chemical characteristics, and because of its special carcinogenic properties. Exposing homogeneous populations of selectively synchronized mammalian cells to this agent offers a novel way to test for alkylation-induced mutations in mammalian cells. These experiments may give us a practical understanding of chemical mutagenesis from alkylating agents which will be useful for estimating total risks, as well as risks relative to other environmental carcinogens, to the human population.

BIBLIOGRAPHIC REFERENCES: R. Goth Goldstein and H.J. Burki. Ethylnitrosourea Induced Mutations in Synchronous and Asynchronous Chinese Hamster Ovary Cells. Mut. Res. 69: 127-137 (1980).

376. ENVIRONMENTAL MUTAGENESIS AND DNA REPAIR

Smith, P. D., Dusenbery, R. L., Emory University, Graduate School, Dept. of Biology, *1364 Clifton Rd. N.E., Atlanta, Georgia*, 30322, United States of America

Mutagen-sensitive (mus) mutants of Drosophila melanogaster are being isolated and characterized for potential alterations in spontaneous and induced mutation frequencies and defects in DNA repair ability. Current studies employ selected monofunctional alkylating agents, which vary with respect to Swain-Scott constants, and include methyl methanesulfonate, ethyl methanesulfonate, methyl nitrosourea and ethyl nitrosourea.

The sex-linked recessive lethal test and the X-linked white eye color locus are being employed to monitor the effect of specific mus loci on alkylation-induced mutation production. Current experiments are focused on the effects of the excision-defective mei-9 and mus(2)201 loci.

In vitro cell culture systems prepared from embryos of wild type and mus strains are being employed to study both

normal DNA synthetic capacity and DNA repair capability following damage by the alkylating agents. Repair studies utilize both autoradiographic determinations of unscheduled DNA synthesis (UDS) and alkaline and neutral sucrose gradient centrifugation to identify specific defects in the repair of alkylation-induced lesions.

BIBLIOGRAPHIC REFERENCES: P.D. Smith, R.D. Snyder and R.L. Dusenbery. 1980. Isolation and Characterization of repair-deficient mutants of Drosophila melanogaster. In DNA Repair and Mutagenesis Eukaryotes (DeSerres, Genceroso and Shelby, eds.) pp. 175-188.

377. SCREENING FOR ENVIRONMENTAL CARCINOGENS BY SHORT-TERM MUTAGENICITY TESTS

Ishidate, M., Sofuni, T., Yoshikawa, K., National Inst. of Hygienic Sciences, Division of Mutagenesis, *1-18-1 Kamiyoga, 1 chome., Setagaya-ku, Tokyo 158, Tokyo, Japan*

OBJECTIVE: To identify potential carcinogens among a wide variety of chemicals in the environment, using short-term mutagenicity tests.

APPROACH: Two different systems - the mutation assay with Salmonella (Ames test) and the chromosomal aberration test with Chinese hamster cells in culture - were used for the evaluation of mutagenicity and/or potential carcinogenicity of chemicals.

PROGRESS: About 300 different compounds, including well-known carcinogens, food aditives, drugs, pesticides and other compounds used in laboratories or industries, have been tested so far. About 89 percent (48/54) and 80 percent (43/54) of the carcinogens tested were positive in the chromosome test and the Ames test, respectively. Out of 75 food additives, only four (potassium bromate, sodium nitrite, sodium hypochlorite and Food Green No. 3) were positive in both tests. Antibiotics, such as actinomycin D, mitomycin C and bleomycin-HCl, were strongly positive in the chromosome test. Positive results were also obtained in several pesticides (captafol, captan, sumithion, malathion, etc.) by both methods. In other chemicals, including beta-propiolactone, styrene oxide, formaline, propan sulton, etc., both tests showed positive results.

378. MUTAGENIC AND CARCINOGENIC EVALUATION OF VINYL CHLORIDE EXPOSURE AND CYTOGENETICS STUDIES

Eftimescu, M., Ministry of Chemical Industry, Labour Protection & Hygiene Centre, Laboratory of Cell Cultures & Genetics, *59 Pop de Basesti, 73244 Bucharest 3, Romania*

The study proposes to monitor cytogenetically some groups of workers professionally exposed to vinyl chloride and to conduct mutagenic studies on Salmonella bacteria. Significant results depending on lengths of exposure have been obtained.

379. EVALUATION OF ORGANIC COMPOUNDS WITH MUTAGENIC AND CARCINOGENIC PROPERTIES PRESENT IN DRINKING WATER

Kool, H. J., van Kreijl, C. F., National Inst. for Water Supply, Chemical Biological Division, *Postbox 150, 2260AD Leidschendam, Netherlands*

In the last decade significant advances have been made in the area of the quantitative and qualitative analysis of organic compounds in drinking water. The increased possibilities of analytical techniques to measure organic constituents have led to the conclusion that the occurrence of these compounds in surface water and in drinking water may create health risks.

In this respect special attention is nowadays paid to those compounds which may cause irreversible changes of the body tissues and for which at this moment threshold limit values cannot be established on a scientific basis, the carcinogens and mutagens.

In the Netherlands a survey of the organic composition of drinking water has been carried out. This study revealed that in drinking water prepared from surface water organic compounds with carcinogenic and mutagenic properties could be detected. For this reason the National Institute for Water Supply (NIWS) started an epidemiological study relating cancer mortality with the presence of organic micropollutants in drinking water of 20 cities in The Netherlands. In connection with this epidemiological study, a preliminary examination for the presence of mutagenic activity in drinking water or surface water was carried out (Ames test). Without using concentration techniques half of the tested samples from the Rhine river were found to have mutagenic activity. Mutagenic activity could be shown in some drinking water after concentrating the organic contaminants by a factor 3000. A further screening of the drinking water in 16 cities is scheduled for 1979/1980.

380. HEALTH ASPECTS OF ORGANICS IN WATER - MUTAGEN SCREENING

Forster, R., Water Research Centre, Medmenham Laboratory, *Hanley Rd., P.O. Box 16, Medmenham SL7 2HD, England, United Kingdom*

OBJECTIVE: The objective of this work is to detect and identify potential carcinogens in drinking water and to determine any relationship between their presence and the degree of wastewater reuse.

APPROACH: Potential carcinogens are to be detected by a bacterial mutagenicity test, and our approach is to screen unconcentrated aqueous samples for mutagenicity: agents can subsequently be identified by fractionation and concentration steps. Freeze concentration, freeze drying, Grob-technique extraction and macroreticular resin absorption have been investigated as possible concentration steps. GC-MS-DP facilities are available to assist with identification.

For mutagenicity testing we are using the Ames Salmonella tester strains in the fluctuation test system developed at the MRC Cell Mutation Unit, University of Sussex. This system increases sensitivity, can be used in conjunction with S9 activation and allows the incorporation of water samples into the growth medium of the test.

Bacterial studies with active fractions are to be followed by in vitro studies using eucaryotic systems.

381. MUTAGENESIS AND CARCINOGENESIS CHARACTERIZATION OF ORGANICS IN DRINKING WATER

Loper, J. C., Smith, C. C., Lang, D. R., University of Cincinnati, College of Medicine, Dept. of Microbiology, *Eden & Bethesda Aves., Cincinnati, Ohio,* 45221, United States of America

OBJECTIVE: Isolation and identification of mutagenic organic molecules from raw and drinking waters. Development of a reproducible column absorption concentration technique. Development of a mutagenesis/transformation assay using human embryonic fibroblast cell cultures.

APPROACH: XAD resin columns are used to concentrate water samples. The analytical work involves solvent extraction and HPLC fractionation methods. The fractions of organic concentrates so obtained are tested for mutagenecity using the Ames Salmonella test. Standard cell culture and mammalian cell mutation techniques are employed in the human fibroblast assay.

PROGRESS: Five cities where water concentrates were shown to contain mutagenic fractions in the acid extracts. HPLC work has shown that the chemical characteristics of these components are probably varied. Current work is in process of isolating these molecules for identification. Definite differences were shown to exist between the mutagenic properties of organic water concentrates from different regions of the country.

382. CARCINOGENICITY OF ALTERNATE DISINFECTANT REACTION PRODUCTS WITH ORGANICS IN DRINKING WATER

Bull, R. J., Pereira, M., Robinson, M., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., Toxicological Assessment Branch, *5555 Ridge Ave., Cincinnati, Ohio,* 45268, United States of America

OBJECTIVE: The carcinogenic potential of of the reaction products of chlorine, chlorine dioxide, combined chlorine and ozone with humic and fulvic acids and other organic material found in surface waters is to be characterized.

APPROACH: A variety of short term in vitro (Ames test) and in vivo (mouse initiation/promotion, hepatic island assays) methods will be used to identify and, it is hoped, quantify hazards associated with disinfection practice.

PROGRESS: Initial experiments have shown that under certain circumstances at least chlorine, chloramines and ozone give rise to carcinogenic by-products. These products are clearly separable from the trihalomethanes.

383. TOXICOLOGY OF COAL TECHNOLOGIES

Reilly, C. A., Norris, W. P., U.S. Dept. of Energy, Argonne National Lab., *9700 S. Cass Ave., Argonne, Illinois*, 60439, United States of America

A multidisciplinary approach was developed for toxicological evaluation of gaseous and particulate effluents from coal combustion, with emphasis on fluidized bed combustion. Effluents from a pressurized and an atmospheric pressure fluidized bed combustor (FBC) in the Chemical Engineering Division were the source of material for chemical and biological asssy. A set of biological test systems was used to assess the activity of FBC fly ash, FBC effluent condensates, and reaerosolized fly ash. Bacterial studies focused primarily on the Ames/Salmonella test. Cultured mammalian cell systems were used to measure cytotoxicity, mutagenesis, and neoplastic transformation. Tissue systems were used to detect hyperplasia and neoplasia, and modifications of the activity of the cytochrome P-450-dependent mono-oxygenase. Mice exposed by inhalation were used to identify tissues and organs at risk. The results were useful in the identification of the many components of coal combustion effluent streams responsible for observable biological effects and potential health effects in man.

384. COAL LIQUEFACTION - MAMMALIAN CELL MUTAGENESIS

Hsie, A. W., U.S. Dept. of Energy, Oak Ridge National Lab., Biology Div., *P.O. Box X, Oak Ridge, Tennessee*, 37830, United States of America

The foremost objective is to screen, and where possible to quantitate, the cytotoxicity and mutagenicity of effluents and crude products from the coal related synthetic fuels, mostly in the form of already identified chemical constituents, or fuel subfractions separated by analytical methods, and, where feasible, the unfractionated synthetic fuel itself. Other objectives are: (1) to study quantitative specified locus mutagenesis by chemicals and radiation, and by the interaction of chemicals and radiation; and (2) to develop a mammalian cell system suitable for simultaneous quantitative analyses of malignant transformation and gene mutations as a means of establishing, ultimately, the possible role of somatic mutation in cancer.

385. COAL LIQUIDS CARCINOGENICITY SCREENING TESTS

Calkin, W. H., E.I. du Pont de Nemours & Co. Inc., *P.O. Box A, Aiken, South Carolina*, 29801, United States of America

The project addresses the potential health effects associated with end use of synthetic liquids produced in 8 different processes under development by DOE. The research is specifically concerned with the crude product, products refined for chemical feedstock as a substitute for natural petroleum and residues after refining. The crude materials and fractions derived therefrom are evaluated for their mutagenic and carcinogenic potential and toxicity by use of a battery of short-term cellular tests and animal bioassay for acute and subacute toxicological effects.

386. DETECTION OF THE ENVIRONMENTAL MUTAGENS AND CARCINOGENS

Nagao, M., Wakabayashi, K., Mori, Y., Yahagi, T., Ministry of Health & Welfare, Biochemistry Div., *5-1-1 Tsukiji, Chuo-ku, Tokyo, Tokyo, Japan*

OBJECTIVE: Detection of the environmental mutagens and carcinogens.

APPROACH: Employing Salmonella mutagenesis testing, we are looking for the mutagens-carcinogens in ordinary foods.

PROGRESS: Mutagenicities of broiled fish and meat, and protein and amino acid pyrolysates were discovered. Structure determination of mutagenic compounds in tryptophan and glutamic acid pyrolysates was made. Mutagenicity of flavonoids was also confirmed and the presence of mutagens in coffee and tea was detected. Co-mutagenic action of norharman and its effect on B(a)P metabolism by microsomal enzymes were elucidated.

387. NEW CELL SYSTEMS FOR THE STUDY OF THE BIOLOGY OF MUTATION AND NEOPLASTIC TRANSFORMATION

Elkind, M. M., U.S. Dept. of Energy, Argonne National Lab., *9700 S. Cass Ave., Argonne, Illinois*, 60439, United States of America

Cultured mammalian cells have many advantages in screening for biological activity in the effluents and by-products of various energy technologies. To begin with, they are closer to mammals than are bacteria, and they are appreciably more economical in time and cost than animal systems. Also, mammalian cells may be used to pursue studies of mechanisms at levels not possible with animals. As cells from different species become available, they may be used to develop extrapolative procedures from mouse to man. Cells of mesodermal origin, specifically fibroblasts, are at present the cell type primarily available for screening purposes. However, because there are only relatively few mesodermal cell lines available for studies of this type, additional cell systems should be established to insure that generalities may be extracted from the collective results. Furthermore, epithelial cell systems are needed for the assessment of mutation and neoplastic transformation since most human cancers originate in epithelium. This program is intended: (1) to establish epithelial- and additional fibroblast-derived cell lines for the measurement of mutation and neoplastic transformation; and (2) to examine the biological mechanisms responsible for expression time after transformation and its relationship to expression time after mutation induction.

BIBLIOGRAPHIC REFERENCES: M.M. Elkin and A. Han, Neoplastic Transformation and Dose Fractionation: Does Repair of Damage Play a Role, Radiat. Res. 79: 233-240 (1979).

388. DEVELOPMENT OF SCREENING METHOD TO DETERMINE POTENTIAL MUTAGENIC AND CARCINOGENIC PROPERTIES

Painter, R. B., University of California, San Francisco Campus, Lab. of Radiobiology, *551 Parnassus Ave., San Francisco, California*, 94122, United States of America

The objective of this project is to develop a rapid test to determine if DNA-damaging agents (potential mutagens and/or carcinogens) are present in energy-related effluents and other materials. Known and suspected agents are briefly incubated with human cells in culture. After removal of the agent, assays for rate of DNA synthesis are made as a function of time, using radioactive precursors of DNA. A decreasing rate of DNA synthesis after removal of the agent indicates the presence of damage in the DNA, whereas no response or an increasing rate of DNA synthesis indicates that no DNA damage occurred and that the agent used was not a mutagenic carcinogen. Validation with a large number of known mutagens and carcinogens and simplification of this test are under way. Recent results include the following: (1) more than 20 chemicals have been screened and the test continues to show promise (an excellent correlation with the Ames test has been demonstrated); (2) HeLa cells are superior to transformed xeroderma pigmentosum cells for the test; and (3) the test is positive even when a chemical that strongly inhibits DNA synthesis but does not damage DNA is in the same sample with a DNA-damaging agent.

BIBLIOGRAPHIC REFERENCES: Painter, R.B., and R. Howard, A Comparison of the HeLa DNA Synthesis Inhibition Test and the Ames Test for Screening of Mutagenic Carcinogens, Mutat. Res. 54: 113-115 (1978).

389. ENVIRONMENTAL CARCINOGENESIS

Anderson, C., U.S. Dept. of Energy, Brookhaven National Lab., *Upton, New York*, 11973, United States of America

Many environmental pollutants that are by-products of energy utilization are suspected of being carcinogens. Screening methods now being employed have one or more deficiencies. This program proposes to evaluate the use of the human virus, adenovirus stereotype 2, for its potential as a rapid method for screening mutagens active in human cells. The specific aims will be to devise a test system for potential carcinogens with the following characteristics: (1) the assay will utilize human cells, (2) the assay will be relatively rapid requiring, at most, 4 to 5 days; (3) scoring of the assay will be capable of automation and will thus allow the unbiased quantitation of results from many samples with little manual labor; and (4) the assay will be

adaptable to biopsy material and may thus allow assessment of risk in individuals or specific populations. The method to be developed would be similar in principle to the widely used Ames test but with human cells instead of bacteria. Mutagenic activity would be ascertained by measuring the reversion of well-characterized viral mutants. Revertants would be identified by virus plaque assay or by an immunofluorescence assay for the synthesis of characteristic viral proteins.

390. METHODS FOR SCREENING ENVIRONMENTAL MUTAGENS

Amzel, V., Johns Hopkins University, School of Hygiene & Public Health, Dept. of Biochemistry, *615 N. Wolfe St., Baltimore, Maryland*, 21205, United States of America

Determination of the carcinogenicty of environmental contaminants is at present accomplished in one of two ways: by in vivo studies utilizing experimental animals or by testing the mutagenicity of the substance in question in bacterial system. The latter method is based on the fact that a striking parallel has been established between carcinogenic and mutagenic agents. Mutagenicity testing in bacterial cells relies on the ability of mutagenic agents to induce reversions of mutations in the histidine operon of Salmonella. Nevertheless, compounds found to be non-mutagenic in bacteria may prove to be mutagenic in a human cell line.

It is the objective of the proposed research to develop methods for the characterization of human somatic cell mutants which can be used to study the effects of potential environmental mutagens. The development of sensitive methods to screen suspected hazardous chemicals with a human 'tester' cell line may be a valuable addition to the bacterial 'tester' system devised by Ames.

I have chosen for this study the hypoxanthine phosphoribosyltransferase (HPRT,E.C.2.4.2.8) system. Mutant and revertant cell lines expressing structural HPRT alterations have been isolated and characterized. In addition, several methods for the selection of cells lacking or expressing HPRT are available. Furthermore, the biochemistry of mutations in the HPRT system is very conveniently studied through the detailed analysis of normal and mutant gene products.

I plan to isolate and characterize stable mutants with an altered HPRT protein in diploid human fibrosarcoma cell line HT-1080. Mutants expressing altered HPRT will be subjected to tryptic and CNBr mapping and amino acid analysis. I plan to develop sensitive micromethods for the analysis of peptides. These methods are: combined chromatography and electrophoresis on thin layer plates, and combined isoelectrofocusing and SDS electrophoresis on polyacrylamide gel slabs. These methods will be used to compare alterations in variant cell lines resulting from exposure to suspected environmental mutagens. I plan to determine the location of the mutation, the amino acid substitution(s), and possibly deduce the nucleotide sequence in the gene.

391. A NEW TEST SYSTEM FOR MUTAGENS BY INDUCTION OF SISTER CHROMATID EXCHANGE IN HUMAN LYMPHOBLASTOID CELLS

Oikawa, A., Tohda, H., Ishiwata, K., Tohoku University, Research Inst. for Tuberculosis & Cancer, Dept. of Pharmacology, *4-1 Seiryomachi, Sendai-shi 980, Miyasi-ken, Japan*

OBJECTIVE: Usefulness of induced sister chromatid exchange (SCE) for detection of environmental and occupational mutagens will be examined. Mutagen activation system (S-9 mix) will be included in the test protocol.

APPROACH: Cell lines to be used are human lymphoblastoid reported in Cancer Research, 38, 253-256; 38, 3560-3562 (1978). Typical mutagen carcinogens of various potencies and their noncarcinogenic analogues will be tested for their SCE-inducing activities. S-9 mix will be prepared from various animals treated with different chemicals, and their properties will be compared.

PROGRESS: EBV-transformed lymphoblastoid cell lines we are using are stable in chromosome number and in number of spontaneous SCE for a long-term culture (so far about 2 years). These properties are suitable for the present purpose.

392. COMPARATIVE MUTAGENESIS

Epler, J. L., Larimer, F. W., Nix, C. E., McKinley, C., Rao, T. K., Waters, L. C., U.S. Dept. of Energy, Oak Ridge National Lab., *P.O. Box X, Oak Ridge Operations Office, Oak Ridge, Tennessee*, 37830, United States of America

The major goal of the Comparative Mutagenesis Unit is to provide a means of mutagenicity testing of those compounds produced by various existing or proposed methods of energy generation through a battery of short-term tests. The work is divided into two phases: one dealing with known compounds expected to occur in the environment through energy production, conversion, or use; and another dealing with actual samples from existing or experimental processes. The benefits to the resource program mission are: (1) screening of test materials from energy-related processes to determine biologically active fractions and compounds to guide; (2) chemical separation and characterization; (3) testing in intact animal systems; and (4) validation of short-term bioassays to predict carcinogenicity and mutagenicity for man.

BIBLIOGRAPHIC REFERENCES: Larimer, F.W., et al., Mutagenicity of N-Nitrosopiperazine Derivatives in Saccharomyces cerevisiae, Mutation Res. 77: 143-148 (1980). Epler, J.L., et al., Energy-Related Pollutants in the Environment: The Use of Short-Term Tests for Mutagenicity in the Isolation and Identification of Biohazards, Environ. Health Perspect. 27: 11-20 (1978).

393. EVALUATION OF POTENTIAL CANCER HAZARDS OF OCCUPATIONAL EXPOSURES BY SHORT-TERM MUTAGENIC ASSAYS

Scassellati Sforzolini, G., Monarca, S., Pasquini, R., Universita degli Studi di Perugia, Facolta di Farmacia, Cattedra di Igiene, *Via del Giochetto, 06100 Perugia, Italy*

Whereas several laboratories have begun using mutagenic screening techniques to test mutagenic activity of single agent, our inferest has been primarily concentrated on a study of the mutagenicity of multiple environmental agents, actually encountered in occupational exposure.

For our research program we have chosen to study the work environment of one industry of an industrialized zone of central Italy which utilizes potentially carcinogenic products such as carbon and petroleum pitches.

Mutagenicity short-term tests by microbial systems are performed either in samples of these products or in air samples collected from working environment (in toto and fractionated), in order to study the feasibility of utilizing these rapid tests to evaluate the mutagenic (and potential carcinogenic) risk of industrial processes. The examined samples are analyzed also for the presence of polycyclic aromatic hydrocarbons.

Besides, epidemiological surveys of exposed workers are carried out and their urine is analyzed to test mutagenic activity using the same microbial short-term tests.

394. MICROBIAL MUTAGENESIS AND PLASMIDS

Mortelmans, K. E., SRI International, Dept. of Microbial Genetics, *333 Ravenswood Ave., Menlo Park, California*, 94025, United States of America

With few exceptions, carcinogens are mutagenic agents that react with and damage DNA. Various physical and chemical agents are known to induce cancer in humans, such as UV-irradiation and vinyl chloride. About 80 percent of all human cancer may be caused by environmental chemical substances, both man-made and naturally occurring.

In recent years, a number of short-term microbial mutagenesis assays have been developed for the detection of chemical mutagens. The most widely used and probably the most reliable microbial mutagenesis test is the Salmonella/mammalian-microsome reverse mutation assay. The test was significantly improved by the introduction of plasmid pKM101 in some of the tester strains. However, the test still does not detect certain classes of carcinogens. The objective of the proposed research is to screen a large number of plasmids to find ones that will be superior to pKM101 or that will supplement pKM101 by making one or more tester strains responsive to known or suspected carcinogens not detected by the test in its present form. Making the test more sensitive will enhance its predictive value for human carcinogenicity induced by environmental mutagens.

395. EFFECTS OF POLLUTANTS ON SOMATIC MAMMALIAN CELLS

Glaser, D. A., University of California, Berkeley Campus, Lawrence Berkeley Lab., *Berkeley, California*, 94720, United States of America

The purpose of this project is to detect and measure the mutagenic and possible carcinogenic effects of a range of environmental pollutants by using highly automated quantitative procedures for the growth of mammalian cells in culture and the identification and isolation of mutant varieties. These techniques permit the measurement of quantitative responses of morphology and growth rate for upwards of 10 to the 6th power growing colonies in single experiments. Chinese hamster, mouse, rat, and human cells, both normal and transformed, will be used. A large number of mutant varieties, particularly having to do with DNA repair capability, have been isolated. The project has been provided guidance that it will be terminated in FY 1981. With reduced funding this year terminal activities towards closeout have started. During the final year we will be cataloging mutant varieties and making these available to other investigators, particularly to Dr. Larry Thompson of Lawrence Livermore Laboratory. All activity will be completed by October 1981.

BIBLIOGRAPHIC REFERENCES: B.D. Aidells, M.W. Konrad and D.A. Glaser, Growth and Morphology of Colonies of CHO Cells Growing on Agar is Affected by Insulin, PNAS 76: 1863-1867 (1979). Aebersold, P., Mutation Induction by 5-Fluorodeoxyuridine in Synchronous Chinese Hamster Cells, Cancer Res. 39: 808-810 (1979).

396. ENVIRONMENTAL MUTAGENESIS TEST DEVELOPMENT PROGRAM (EMTDP)

Zeiger, E., Walters, D., Margolin, B., Mason, J., Resnick, M., Rowley, M., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Environmental Health Sciences, Laboratory of Molecular Genetics, *P.O. Box 12233, Research Triangle Park, North Carolina*, 27709, United States of America

The objectives of the Environmental Mutagenesis Test Development Program are twofold. The first is the development of an integrated program for the routine testing of large numbers of chemicals for mutagenicity. This includes such diverse factors as test-system validation, identification and development of new test methods, development of an increased understanding of mutagenesis and development of a strategy and an organizational structure for conducting a large scale testing program and interpreting the results obtained. The second objective is implementation: to test up to 1000 commercial and environmental chemicals per year for mutagenicity.

BIBLIOGRAPHIC REFERENCES: Zeiger, E. (1979) Mammalian cell mutagenesis in a mutagen screening program. In Banbury Report No. 2, Mammalian Cell Mutagenesis: The Maturation of Test Systems. Ed. A Hsie, J.P. O'Neill and V.K. McElheny, pg. 145-153.

397. SCREENING SELECTED RIVERS IN MASSACHUSETTS FOR MUTAGENIC (AND PRESUMABLY CARCINOGENIC) POLLUTANTS WITH PLANT AND MICROBIAL BIOASSAYS

Klekowski, E., University of Massachusetts, Amherst Campus, School of Arts & Sciences, Dept. of Botany, *Amherst, Massachusetts*, 01002, United States of America

The Housatonic, Chicopee, Whitman, and Nashua Rivers in Massachusetts will be monitored for mutagenic (and presumably carcinogenic) pollutants. In situ plant bioassays based upon measurements of mutational damage in native riparian plant populations will be the basis of a broad watershed survey, and microbial mutagen assays will be employed to intensively study specific areas.

C. OTHER IN VITRO TESTS

398. AIR POLLUTANTS ON LUNG AIRWAY CELLS IN NOVEL CULTURE

Crocker, T. T., Rasmussen, R. E., University of California, Irvine Campus, California College of Medicine, Dept. of Community & Environmental Medicine, *Irvine, California*, 92664, United States of America

Using a unique exposure system which enables direct exposure of cultured cells to air pollutants, this project will determine the acute and long-term effects of exposure to pollutant gases on primary and secondary cultures of mammalian respiratory cells obtained from fetal and adult rat tissue. Cell types will include tracheal epithelial cells, type II alveolar cells and alveolar macrophages. Cells grown on Millipore filters and fed from the reverse side will be exposed to atmospheres containing the common air pollutant gases, NO2, SO2, and O3. Parameters to be measured are cell viability, function and macromolecular synthesis. Specific experiments will be done to examine possible co-carcinogenic effects of these gases. The exposure system may enable the detection of synergistic effects of pollutant mixtures which heretofore have not been measurable. The ability to expose cells directly to the atmosphere for prolonged periods will enable the discovery of possible long-term effects.

399. ASBESTOS-INDUCED DNA DEGRADATION

Vincent, R. A., Medical University of South Carolina, School of Medicine, Dept. of Pathology, *80 Barre St., Charleston, South Carolina*, 29401, United States of America

Chronic breathing of airborne asbestos fibers, which may be difficult to avoid in shipyards and other sites where construction and repair of fire-proofed structures are carried out, carries a high risk of cancer. Similar fibers of glass or quartz do not present an equal hazard. It may be presumed that asbestos fibers have a physiological action which needs to be explained. Since the lesions produced by the fibers tend to develop into malignancies, it is reasonable to expect this action to involve the DNA within the cells. It is the objective of this research to study the damage produced in cultured cells through observation of DNA degradation and repair.

Normal human fibroblastlike cells will be cultured and radiolabelled with thymidine. The effects of particles of different composition and size will be determined with respect to the release of the radio-label. Other evidence of the effect of the DNA within the cells will be measured by DNA sedimentation in alkaline sucrose gradients, correlation of radio-label release with release of lysosomal enzymes, and determination of strand breakage in the DNA. The chemical form of the released radio-label will also be determined.

400. DNA DAMAGE BY CHEMICAL CARCINOGENS AND ITS REPAIR IN HUMAN CELLS

Fornace, A., Lechner, J., Harris, C., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst., Human Tissue Studies Section, *9000 Rockville Pike, Bethesda, Maryland*, 20205, United States of America

Our initial studies have involved the effect of asbestos and several metal carcinogens, which are often present in trace levels in asbestos, on DNA in human cells. With the alkaline elution technique, DNA-protein crosslinks were detected in fibroblasts exposed to chromate salts. No evidence of repair was seen with up to 12 hours repair incubation after chromate removal from the culture medium. Using an in vitro assay, DNA-protein crosslinks were also detected. In the case of asbestos and nickel, no DNA damage was seen after exposure of fibroblasts to these agents. With the development of methods to maintain human bronchial epithelial cells in culture, DNA damage and repair studies are now being initiated with these cells with particular emphasis on agents implicated in pulmonary carcinogenesis.

401. MINERAL FIBER SIZE AND CARCINOGENICITY IN VITRO

Frank, A. L., City University of New York, Mount Sinai School of Medicine, School of Medicine, Dept. of Community Medicine, *1 Gustave L. Levy Pl., New York, New York*, 10029, United States of America

The objective of the research is to ascertain whether the size of mineral fibers such asbestos and fibrous glass is a determinant of the development of cancer as assayed by epithelial cell responses in vitro. Tracheal explants are maintained in chemically defined culture medium and fibers to be studied are added. Hyperplastic changes are noted and quantitated using image analysis equipment. The accuracy of hyperplasia induced in this culture system as a predictor of neoplasia is to be evaluated.

402. LOW BTU GASIFIER - EARLY DAMAGE INDICATORS FOR INHALED EFFLUENTS

Mitchell, C. E., Lovelace Center for the Health Sciences, *5200 Gibson Blvd. S.E., Albuquerque, New Mexico*, 87108, United States of America

Potential health risks associated with low Btu coal gasification have not been adequately evaluated. Extensive literature has demonstrated the carcinogenic properties of various substances associated with the processing and utilization of coal and, although the products of coking, petroleum refining, coal pyrolysis and coal combustion are not identical to those of coal conversion, similar compounds may also be present in coal conversion processes. To assess the risks that may be associated with this developing technology and to provide guidance for developing cleanup systems, a project has been initiated to evaluate the relative cytotoxicity, mutagenicity, and carcinogenicity of various effluents from low Btu gasifiers. A multi-tiered approach is being utilized whereby initial in vitro screening of effluents is done using bacterial and mammalial screening procedures. Selected materials found potentially hazardous from in vitro tests will be further evaluated in whole animal inhalation studies. Changes in lung cell biochemical function will be assessed and compared with histologic alterations occurring at similar times after inhalation exposure. Of primary interest will be the relative carcinogenicity of materials studied. It is anticipated that results from these studies will assist in the establishment of adequate health protection standards and identification of required control technologies.

403. H-COAL, CELL SCREENING

Epler, J. L., Larimer, F. W., Rao, T. K., U.S. Dept. of Energy, Oak Ridge National Lab., *P.O. Box X, Oak Ridge Operations Office, Oak Ridge, Tennessee*, 37830, United States of America

The objective of this biological screening is to provide early information on the potential biohazards unique to liquefaction operations. A battery of short-term bioassays will be applied to selected process samples including product oils, aqueous discharges, and solid wastes. Tests in the cellular bioassay category will (1) act as predictors of profound long-range health effects such as mutagenesis and/or carcinogenesis, (2) act as a mechanism to rapidly isolate and identify a hazardous biological agent in a complex mixture, and (3) function as a measure of biological activity correlating baseline data with changes in process conditions. Assuming that the complex mixtures can be fractionated and approached in these short-term assays, we will accumulate information reflecting on the actual compounds responsible for the biological effect and/or biohazard. Thus, tests in this category will aid in the identifying the specific hazardous compounds involved and relegate priorities for further validative testing, testing whole animals, and more definitive chemical analysis and monitoring.

404. EFFECTS OF VITAMIN C OR L-CYSTEINE ON CELLULAR GROWTH AND SURVIVAL TIME OF NORMAL ADULT LUNG TISSUE IN CULTURE

Leuchtenberger, C., Leuchtenberger, R., Inst. Suisse de Recherches Experimentales sur le Cancer, Dept. of Cytochemistry, *Chemin des Boveresses, rue Bugnon 21, CH1066 Epalinges, Lausanne, Switzerland*

OBJECTIVE: Well-growing cultures prepared from normal adult human tissues are a very much needed model system for screening and assessment of short- and long-term biological activity of environmental suspected and known carcinogenic agents. However, the short survival time of normal adult human tissue cultures presents an inherent difficulty in the establishment of such a model system. We found this feature to be a decided disadvantage in our experimental studies on adult human lung cultures, in which we were trying to answer the important question of whether early alterations such as abnormalities in DNA, cell division, growth and number of chromosomes, observed after short-term exposure to either tobacco or marihuana smoke, would be followed, after long-term exposure to smoke, by malignant transformation. For this reason an attempt was made to prolong the life span of cultures from normal adult human lung tissue by adding naturally occurring metabolites to the media, such as L-cysteine or vitamin C.

APPROACH: Cultures from normal adult human lung were prepared as previously described and grown in Eagle-Dulbecco media with and without addition of either L-cysteine or vitamin C. The cultures were divided into non-exposed control cultures and cultures exposed to fresh smoke from either tobacco or marihuana cigarettes, as previously described.

PROGRESS: There were significant differences in cell morphology, growth rate, and survival time between control cultures grown in normal media, and those grown in normal media to which either L-cysteine or vitamin C had been added. The latter cultures showed a striking increase in lysosomes and epitheloid cells already after one week. Furthermore, these cultures became similar to the original lung tissue itself, and it was possible to prepare continuous subpassages. The life span of these cultures was significantly increased (92 weeks) while the cultures grown in media without L-cysteine or without vitamin C died within a period of 12-16 weeks. There were no significant differences between non-exposed control cultures grown in media with L-cysteine or vitamin C, and those grown in the same media after exposure to smoke from either tobacco or marihuana cigarettes.

405. SOLID STATE RADIOIMMUNOASSAY IN COCARCINOGENESIS

Kennel, S. J., U.S. Dept. of Energy, Oak Ridge National Lab., Biology Div., *P.O. Box X, Oak Ridge, Tennessee*, 37830, United States of America

The focus of this project is the development of solid state radioimmunoassays that will be useful in screening of clones of cells for transformed phenotypes. Altered gene regulation, characteristic of transformation, causes expression of proteins unique to tumor cells. Conventional analysis of cell proteins from individual clones in carcinogen treated cultures is expensive and laborious. Protein quantitation by radioimmunoassay can be automated using solid state secondary antibodies. This automation allows analysis of large numbers of cell clones for proteins associated with transformation, providing quantitation of the frequency of altered gene expresion. Specifically, radioimmunoassays for leukemia virus protein will be used to perfect the solid state technology. Frequencies of viral gene expression will be measured in cell populations treated with chemical carcinogens. Subsequently, assays for plasminogen activator and tumor specific antigens will be used to study transformation of epithelial cultures. The cell system of rat tracheal epithelium shows promise in this study since many tumors from these cell populations bear cross-reactive antigens potentially useful for screening purposes. Exploiting advantages for screening clones using solid state radioimmunoassays provides an objective approach to evaluating the involvement of chemical by-products of energy production in altering gene expression.

406. CYTOLOGIC AND METABOLIC EFFECTS OF ONCOGENS

Crocker, T. T., Rasmussen, R. E., University of California, Irvine Campus, California College of Medicine, Dept. of Community & Environmental Medicine, *Irvine, California*, 92664, United States of America

The purpose of this fundamental research is to characterize metabolic pathways of selected Air Force chemicals in animal and human derived tissues to provide data for estimating whether man metabolizes compounds like sensitive or resistant animal models; to examine cells from animals and man for recognition of cellular abnormalities, chromosome changes, and the capacity to respond in vitro to carcinogenic or mutagenic materials; to identify the capacity of cells to incorporate, metabolize or bind these materials; to identify neoplastic and mutagenic transformation of mammalian cells and microorganisms.

Cytologic studies will encompass: (1) observation and quantitation of chromosome and nuclear abnormalities in peripheral lymphocytes and bone marrow of exposed animal models, (2) early detection of mutagenesis or induction of neoplasms in exposed models, (3) measurement of carcinogen-metabolizing enzyme levels in cells and tissues of exposed models, and (4) DNA repair activity of exposed cells. Metabolic pathways of selected compounds will be studied in appropriate models to assess the ability of the compounds to act as direct or indirect alkylating agents. The processes are necessary to make valid extrapolations of oncogenic potential to man from animal data.

D. IN VIVO SYSTEMS

407. CARCINOGENICITY OF DIMETHYLFORMAMIDE - NCI

Kommineni, C., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Biomedical & Behavioral Science, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

Dimethylformamide (DMF), a water miscible, highly polar solvent is used widely in chemical, pharmaceutical, resin and polymer industries and added to gasoline to prevent carburetor icing. The population at risk is estimated at 45,660. Workers over-exposed to DMF have exhibited a myriad of symptoms - cyanosis, confusion, dizziness and gastrointestinal disorders leading to colicky pain. Workers exposed to DMF who also consume alcohol manifested facial flushing. This suggests that the blood levels of alcohol and acetaldehyde of such workers may be altered. DMF was also incriminated in causing liver and pancreatic damage in humans. Dr. Kommineni, 1972, found that intraperitoneal injections of DMF induced epithelial and non-epithelial neoplasms of gastrointestinal tract in rats. This observation is of major interest in relation to the supposed conversion of colonic adenomatous polyps to carcinomas in humans.

The purpose of this inhalation study is to determine the long-term biological and possible carcinogenic effects of DMF in rats and monkeys. Two dose levels will be selected for chronic 18-month exposures. Animals will be held six months post-exposure to maximize tumorigenesis. Monkeys will essentially be used to monitor the effects of DMF on liver and pancreas. Rats will be sacrificed on a serial schedule and morphological and biochemical alterations (SGOT, SGPT, AP, SOCT-serum ornithinecarbamyl transferase, SSDH-serum sorbitol dehydrogenase, serum and fecal lipase and amylase) monitored. Blood from monkeys will be drawn also (without sacrifice) for serum enzyme analysis. A representative number of exposed animals will receive ethanol in drinking water and blood alcohol and aldehyde levels (along with the serum enzyme levels) will be determined. Data developed from this contract study will be incorporated with that developed on DMF under the National Toxicology Program.

408. CARCINOGENICITY OF AROMATIC AMINES - AZO DYES

Lewis, T., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Biomedical & Behavioral Science, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

The purpose of this project is to compare and contrast the carcinogenic potential of two aromatic-azo dyes - disperse yellow 3 and acid black 52 - using the intratracheal and feeding routes of administration. Epidemiologic studies have revealed increases in the incidence of bladder tumors in workers exposed to aromatic-azo dyes above those of the general population and this study will investigate these epidemiological findings using laboratory rats and hamsters.

NCI is currently investigating or planning to study the carcinogenicity of 3 benzidine azo dyes of commercial significance -direct black 38, direct blue 36, and direct blue 218 - as well as certain other azo dyes in feeding studies. The two dyes selected in this study represent chemical structures whose carcinogenic activity is difficult to predict when inhalation and dermal are the primary routes of exposure, rather than the oral route. Bladder implants of disperse yellow 3 and oil orange SS, a compound having a chemical moiety similar to one found in acid black 52, have produced carcinomas of the bladder.

The population at risk from exposure to disperse yellow 3 and acid black 52, respectively, includes 3929 and 1207 workers in the dye industry. Production figures from the U.S. Tariff Commission indicate that 1,161,000 pounds and 762,000 pounds of disperse yellow 3 and acid black 52, respectively, were produced in the United States in 1976. This study is being conducted by contract (210-78-0032). Acute and subchronic range-finding studies have been completed. Chronic (18-month) administration of dyes is scheduled to begin in the first quarter of FY 80.

409. CO-CARCINOGENICITY OF ENVIRONMENTAL METALS AND MINERALS WITH SYSTEMIC CARCINOGENS IN THE RAT LUNG (ABBREV)

Heath, J. C., Strangeways Research Lab., Dept. of Cancer Research, *2 Wort's Cswy., Cambridge CB1 4RN, England, United Kingdom*

OBJECTIVE: To investigate the carcinogenic action of very small lung deposits of mixed particulate minerals and metals of environmental importance, acting alone or together with a very low level of a systemic carcinogen.

APPROACH: The particulate minerals and metals are administered in a small amount by a single intratracheal instillation under anaesthesia. After about 6 weeks, when the pulmonary lesion is well established, a short course of once-weekly subcutaneous injections of a very low dose of a systemic carcinogen such as a nitrosamine is given. No further treatment is given, and the animals are allowed to live out their lives or to live until increasing respiratory distress renders their destruction desirable. The lungs and other relevant internal organs of all rats are fully examined postmortem.

PROGRESS: Lung lesions induced by minimal deposits of particulate silica or fibrous asbestos only very occasionally proceed to malignant metastasizing lung tumors. With the concurrent action of particulate cobalt, nickel or cadmium metals at 10% w/w of the total lung particulate deposit, rather more malignant lung tumors are produced. The further administration of a very low level of a systemic carcinogen such as a nitrosamine, acting systemically but at a level low enough not to induce a significant number of malignant lung tumors by itself, can increase significantly the incidence of such tumors.

410. ETIOLOGIC CO-FACTORS IN ASBESTOS-CARCINOGENESIS

Brand, K. G., Brand, I., University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Microbiology, *1305 Mayo, Minneapolis, Minnesota,* 55455, United States of America

We are attempting to explore factors and events involved in asbestos-cancer. Ivalon R sponge matrices containing asbestos fibers are implanted into the pleural cavities of mice. The carcinogenic process will be followed and analyzed employing a methodology which we have previously developed for the study of foreign body tumorigenesis. Specifically, the following questions regarding asbestos carcinogenesis will be investigated: Cell type of tumor origin; frequency of preneoplastic foci; morphological and cultural characteristics of preneoplastic cells; their mono- or pluriclonal origination and expansion; preneoplastic kinetics and maturation stages at the tissue and cellular levels; timing and nature of physical interaction between asbestos fibers and cells at various defined stages of the carcinogenic process; the role of tissue fibrosis and phagocytic macrophage activity. In view of the fact that asbestos and other tumorigenic fibers cannot easily be eliminated from the environment of an industrial society, we need a deeper and detailed understanding of the carcinogenic process in asbestosis if we want to approacch prevention and cure by different and additional means.

BIBLIOGRAPHIC REFERENCES: V.J. Michelich and K.G. Brand. Gonadectomy affecting foreign body tumorigenesis in CBA/H mice. J. Natl. Cancer Inst. 64:807-808, 1980. K.G. Brand and I. Brand. Cancer from asbestos, schistosomiasis, and cicatrization. Zbl. Bakt. I. Abt. Orig. B. 171:1-17, 1980.

411. EFFECTS OF INGESTED ASBESTOS IN HAMSTERS

Shefner, A. M., I I T Research Inst., *10 W. 35th St., Chicago, Illinois,* 60616, United States of America

The Contractor shall endeavor to determine if lifetime oral ingestion of asbestos is carcinogenic or produces other pathologic effects and assess what interaction, if any, occurs between a carcinogen known to induce bowel cancer and oral ingestion of asbestos using 2 abestiform types in hamsters.

412. BIOLOGICAL EFFECTS OF INGESTED ASBESTOS IN RATS

Rutter, H. A., Hazleton Lab. America Inc., *9200 Leesburg Tpke., Vienna, Virginia,* 22180, United States of America

The contractor shall attempt to determine if lifetime oral ingestion of asbestos is carcinogenic or produces other pathologic effects and assess what interaction, if any, occurs between a chemical carcinogen known to induce bowel cancer and oral ingestion of asbestos, using four asbestiform types in rats.

413. CARCINOGENIC POTENTIAL OF ARSENIC COMPOUNDS IN DRINKING WATER

Lakso, J. U., Shirachi, D. Y., University of the Pacific, School of Pharmacy, *3601 Pacific, Stockton, California*, 95204, United States of America

OBJECTIVE: Utilizing short-term in vivo methods, the activity of various forms of arsenic as tumor initiators, promoters and carcinogens will be evaluated. The experiments planned will evaluate individual species of As to determine which is the critical form(s) to be regulated and to arrive at a reasonable level for regulation.

APPROACH: The present study will employ an initiation/promotion assay which utilizes preneoplastic lesions in the liver as the first test system. This system has been previously used with a variety of chemical carcinogens by HERL-Cincinnati with the methodology suggested. Because As effects on other systems have been documented in humans, some limited exploratory work is to be taken up in alternative systems including the mouse lung adenoma system.

414. TOXICOLOGY OF KRYPTON-85

Ballou, J. E., U.S. Dept. of Energy, Battelle Pacific Northwest Lab., *P.O. Box 999, Richland, Washington*, 99352, United States of America

Krypton-85 is a radioactive noble gas effluent that is released to the environment principally during the dissolution-processing of nuclear fuel elements. Since 85Kr is one of the few intentional effluents of the nuclear process that is radioactive, the health impact of this material is of major interest to DOE. The objective of this research is to provide biological information to supplement earlier, more theoretical evaluations of the health hazards of 85Kr exposure. This project will include both short-term and chronic exposure studies, in several species, to determine tissue distribution and retention kinetics for metabolic modeling purposes (as well as long-term biological effects studies) for purposes of defining the tissues at risk. Also included are dose-effect studies to determine tumorigenicity, teratologic potency, and capacity to induce changes in lung biochemistry and hematopoiesis.

415. HEALTH EFFECTS - KRYPTON

Kirk, W. P., U.S. Environmental Protection Agency, Health Effects Research Lab., *Research Triangle Park, North Carolina*, 27711, United States of America

To define the biological hazard from Kr-85 released to the environment, experimental animals are being exposed to a cloud of Kr-85. The study will evaluate the long-term effects of acute exposure in guinea pigs and acute and chronic exposure of rats. The distribution, rate of removal, the dose to several organs, and the acute LD/sub 50-30/ for inhalation exposure were determined in guinea pigs. Following this evaluation, rats, Chinese hamsters and guinea pigs were exposed in beta-infinite geometry to determine the acute LD/sub 50-90/. Life time observation to evaluate long term hazards is in progress on guinea pigs surviving the LD/sub 50/ study and rats exposed in a skin-tumor induction study. Rats will be exposed in utero and chronically postnatally to Kr-85 in beta infinite geometry at multiples of the occupational MPC/sub a/. Preliminary data indicate an excess of lymphocytic leukemias in female guinea pigs.

416. TOXICITY OF PU-239 AND RA-226

Jee, W. S., Utah Higher Education System, University of Utah, School of Medicine, Dept. of Anatomy, *1400 E. 2nd S., Salt Lake City, Utah*, 84112, United States of America

The objective of this project is to assess the toxicity of plutonium in man. Beagles are injected intravenously at 17 months of age with Pu-239 or Ra-226, and observed throughout their lifespan for radiation-induced lesions, which occur primarily in the skeleton and liver. The major radiation induced endpoint encountered is skeletal cancer, occurring from 2 to 13 years after injection. The lifespan of beagles in this laboratory averages approximately 13 years. Detailed retention studies are used to calculate radiation doses. Detailed quantitative histopathologic studies are performed so that beagle and human skeletons can be compared and tumor incidence in beagles can be used to improve risk estimates in man.

417. DEVELOP AND APPLY THE HEMOGLOBIN BINDING ASSAY TO CHEMICALS IN DRINKING WATER ASSESSING RELATIVE PHARMACOKINETIC QUESTIONS

Chang, L., Lin, H. L., Guion, C., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio*, 45268, United States of America

OBJECTIVE: The relationship for chemicals found in drinking water of their binding to hemoglobin as a measure of internal dose and their carcinogenic potency will be applied to the question of across-species extrapolation of carcinogenic hazard.

APPROACH: The binding of chloroform and other components of drinking water to rat and mouse hemoglobin will be determined. The carcinogen potency of drinking water and its components including chloroform will be estimated by short-term bioassays, including the rat liver island assay, and by their binding to and damage of target organ DNA.

PROGRESS: The pharmacokinetic parameters of chloroform binding to rat hemoglobin have been determined for oral exposure. We have developed the rat liver island assay and are testing drinking water concentrates. The alkaline elution assay for DNA damage is under development. The binding of radiolabeled chloroform to liver and kidney DNA is being determined.

418. CARCINOGENICITY OF ALTERNATE DISINFECTANT REACTION PRODUCTS WITH ORGANICS IN DRINKING WATER

Bull, R. J., Pereira, M., Robinson, M., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., Toxicological Assessment Branch, *5555 Ridge Ave., Cincinnati, Ohio*, 45268, United States of America

The summary for this project is under entry no. 382.

419. HEPATIC ISLAND ASSAY OF CHEMICAL CARCINOGENS FOUND IN WATER

Pereira, M. A., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio* 45268, United States of America

OBJECTIVE: The rat liver island assay will be validated with chemical carcinogen and promotor present in drinking water.

APPROACH: The dose response relationship of chemical carcinogens found in drinking water will be determined in the rat liver island assay. The assay will also be modified in order to test for the presence in water of tumor promotors.

PROGRESS: A study of the ability of chloroform to initiate and/or promote rat liver islands has been started.

420. REPRODUCTIVE HAZARD ASSESSMENT OF STYRENE MONOMER - NCI

Hardin, B., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Biomedical & Behavioral Science, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Styrene is extensively used in the manufacture of a wide variety of rubber and plastic products. Over six billion pounds of styrene were produced in the U.S. in 1977, with an estimated 50,000 workers exposed. The present Federal occupational exposure limit for styrene and the TLV currently recommended by the American Conference of Governmental Industrial Hygienists is 100 ppm (420 mg/cubic meter).

When developing a criteria document for styrene, NIOSH found only 2 investigations of the effects of styrene on reproduction. A Soviet study reported increased fetal and post-natal mortality following daily 4-hour exposures as low as 1.5 mg/cu. m. An American study reported no adverse effects following exposure of pregnant rats and rabbits at concentrations as high as 2520 mg/cu. m. Both studies appeared to be sound, but differences in test protocols prevent a direct comparison of the results. Styrene has not been adequately tested for carcinogenic potential. In one unpublished study, there was some evidence of an increased incidence of tumors following long-term inhalation exposure to styrene, but several difficulties in this study reportedly made firm conclusions impossible.

The objectives of this contract effort are twofold. One objective is to test styrene under conditions that will permit verification of the Soviet study. The second objective is to observe rats exposed to styrene in utero, for possible transplacental carcinogenic effects. Confirmation of postnatal effects reported by the Soviets requires that some rats be allowed to deliver and raise their litters to weaning. Maintaining these offspring for their lifetime offers the opportunity to screen for transplacental carcinogenic effects without the added expense of repeating the inhalation exposures.

421. ENVIRONMENTAL PERYLENE AS A POSSIBLE CARCINOGEN

Anderson, R. S., Sloan Kettering Inst. for Cancer Research, *145 Boston Post Rd., Rye, New York*, 10580, United States of America

OBJECTIVE: The overall objective of the proposal is to use the salamander Ambystoma trigrinum as a model organism to assess the carcinogenic/co-carcinogenic potential of perylene.

APPROACH: Our collaborative approach is essential for answering questions concerning the biological activity of perylene in Ambystoma. The collecting, maintaining, and in vivo carcinogenesis studies will be carried out in Texas under the direction of Dr. Rose. He first described the neoplastic lesions in Ambystoma from Reese AFB, and also has extensive experience in laboratory studies of these animals. The progression of all gross cutaneous lesions will be recorded photographically. Biochemical research will be conducted at Sloan-Kettering Institute by Dr. Anderson.

422. DEVELOPMENT OF A CARCINOGEN ASSAY SYSTEM UTILIZING ESTUARINE FISHES

Martin, B. J., University of Southern Mississippi, School of Science & Technology, Dept. of Biology, *Hattiesburg, Mississippi*, 39401, United States of America

OBJECTIVE: The objective of the proposal is to continue development of a carcinogen assay system using aquatic organisms.

APPROACH: Efforts will be continued to determine the LC-50 of BEN with respect to both juvenile and adult Cyprinodon. Exposures of Cyprinodon and Ictalurus to BEN and DENA will be repeated with weekly contaminations at 1 ppm. Similar experiments will also be conducted at a somewhat lower level of exposure.

423. DETERMINATION OF THE CHRONIC MAMMALIAN TOXICOLOGICAL EFFECTS OF TNT

Lish, P. M., I I T Research Inst., *10 W. 35th St., Chicago, Illinois*, 60616, United States of America

OBJECTIVE: To determine the mammalian chronic toxicity and carcinogenicity of TNT to provide data for the development of effluent guidelines for TNT from Army-owned ammunition plants.

Studies will be performed to determine the chemical-biological interaction of TNT for chronic exposures to mammals. This will include assessments for carcinogenicity and teratogenicity. Also, detailed metabolic studies will be conducted to identify target organs.

424. INHALATION CARCINOGENESIS OF ENVIRONMENTAL AGENTS

Albert, R. E., New York University, School of Medicine, Dept. of Environmental Medicine, *100 Washington Sq. E., New York, New York*, 10003, United States of America

This is a program project grant proposal which involves a series of studies that concern major current problems in the carcinogenic action of important environmental (including occupational) agents by the inhalation route. These studies deal with mechanisms of action of carcinogens, development of animal models, dose-effect relationships, and interactions of environmentally important agents in the carcinogenic process. The six proposed studies involve the relationship of structure to carcinogenic function of acylating agents, the cocarcinogenic action of catechol and benzo(a)pyrene, the development of an animal model for leukemogenesis by benzene and lung cancer by arsenic trioxide, the carcinogenic interaction of hydrogen chloride and formaldehyde, and the relationships of fiber length to the inhalation carcinogenicity of asbestos. The proposal also includes support for Core Unit to operate the inhalation facility and renovation to upgrade the safety of carcinogen handling in the inhalation facility.

425. CARCINOGENESIS TESTING OF ENVIRONMENTAL CHEMICALS

Kurokawa, Y., Maekawa, A., Takahashi, M., Kokubo, T., Ogiu, T., Hayashi, Y., National Inst. of Hygienic Sciences, Division of Pathology, *1-18-1 Kamiyoga, 1 chome., Setagaya-ku, Tokyo 158, Tokyo, Japan*

OBJECTIVE: To detect environmental carcinogens which might be the cause of human cancers.

APPROACH: At first, subacute toxicity studies of the effects of chemicals on rats are performed. Depending upon the maximum tolerated dose (MTD) obtained from the subacute studies, 2-year carcinogenesis studies using rats are to be started . The results are to be evaluated after complete autopsy and histological examination.

PROGRESS: Chemicals under investigation are: potassium bromate, hydrogen peroxide, thiram, sodium hypochlorite, caramel, piperonyl butoxide and retinyl acetate.

426. COAL-OIL MIXTURES TOXICOLOGY

Raabe, C., University of California, Davis Campus, Graduate School, *Davis, California*, 95616, United States of America

The summary for this project is under entry no. 354.

427. INHALATION TOX SHALE DUST

Holland, L. M., U.S. Dept. of Energy, Los Alamos National Lab., Health Div., Mammalian Biology Group, *P.O. Box 1663, Los Alamos, New Mexico*, 87544, United States of America

The long-term goals of this relatively new program may be summarized as follows: (1) obtain samples of the potentially hazardous materials associated with oil shale mining and various processing stages and prepare them in a form suitable for exposure of small laboratory animals; (2) expose the animals by the relevant routes and study both nonlethal and lethal toxic effects; (3) determine by chemical analysis the tissue distribution of the applied substances, possibly including their metabolic products; (4) observe tissues microscopically and biochemically to determine the site and mode of toxic action, including tumor formation; and (5) assess the results in terms of existing or proposed acceptable exposure limits for the workers and the population. The description of the detailed program will follow this order of scientific progression. Short-term inhalation exposures of Syrian hamsters to both raw and spent shale were begun in mid-1976. Longer term inhalation studies (up to 60 weeks) were initiated in 1977 with raw shale and two kinds of spent shale. Aerosols were generated from a Wright dust feed after material obtained from the Laramie Energy Research Center (LERC) was reduced to a fine dust by ball-milling. In an effort to deliver more precise doses and to enhance the response, several groups of animals were also exposed to suspensions of the same aerosolized shale material by intratracheal instillation. Long-term dermal carcinogenicity studies which compare crude shale oils with standard petroleum crude oils are in progress. Experiments involving intestinal tract exposure have also been initiated. Fibrogenesis and carcinogenesis are the biomedical end points of primary interest in this program and will be studied by standard methods (e.g., histopathology, histochemistry, hematology, and blood chemistry). Immunological competence will also be tested.

428. FBC - CHRONIC RESPIRATORY DISEASE FROM INHALED EFFLUENTS

Mauderly, J. L., Lovelace Center for the Health Sciences, *5200 Gibson Blvd. S.E., Albuquerque, New Mexico*, 87108, United States of America

The primary mode of human exposure to FBC effluents is expected to be chronic inhalation over varying periods of time ranging to lifespan. The extent to which these exposures may result in chronic lung disease is largely unknown, although the effluents contain known irritants, cytotoxic agents and possibly carcinogens. Animals will be exposed by inhalation to components of FBC or conventional coal combustion and evaluated by functional and morphological endpoints to study the occurrence and nature of any lung disease produced. Studies will initially focus on rodents exposed to fly ash, trace metals and hydrocarbons. Subsequent exposures may include these materials in combination with irritants such as SO2 and NO2. Endpoints will

include lifespan shortening, functional disorders and structural changes, including carcinogenesis. More detailed, mechanistic studies will be initiated as appropriate to study specific disease processes. The effect of pre-existing disease in modifying responses will be studied using animal models of emphysema, asthma and fibrosis. Effort to date has been largely directed toward development of exposure methodology, biological assessment systems, and disease models.

BIBLIOGRAPHIC REFERENCES: Mauderly, J.L., Lung-Thorax System, Section VI-A in Handbook of Aging: Physiology, E.J. Masoro (ed.), CRC Press, Inc., West Palm Beach, Fl, 1978.

429. FBC - KINETICS OF LUNG CELLS IN RESPONSE TO INHALED EFFLUENTS

Hackett, N. F., Lovelace Center for the Health Sciences, *5200 Gibson Blvd. S.E., Albuquerque, New Mexico*, 87108, United States of America

Conventional coal burning power facilities emit effluents that produce acute lung disorders at high concentrations and minimal damage at lower concentrations. Fine particulates in these effluents which serve as condensing surfaces for aerosols of volatile trace heavy metals and organics can carry these potentially hazardous agents into the deep lung. Biological indicator systems are needed for rapid in vivo screening of cytotoxicity, mutagenicity and carcinogenicity. Cytokinetic techniques provide a sensitive indicator of lung cell damage as cellular proliferation is the primary means by which pulmonary injury is repaired. Autoradiographic methods indicate differential injury effects on various cell populations by evaluation of (1) increased cell renewal, (2) rate of cell replacement, and (3) duration of repair sequence following an acute inhalation exposure. Cytokinetic evaluation of cell proliferation will be applied during chronic exposures and will be used to determine possible synergistic action of mixtures of pollutants. Histochemical and cytochemical methods will enhance evaluation of cellular interaction mechanisms of damage and repair. Cell replacement will be correlated with physiologic and pathologic changes to assess the relationship between cell division and development of specific pulmonary diseases.

430. RESPIRATORY CARCINOGENESIS OF DIESEL FUEL EMISSIONS AND RELATED SUBSTANCES

Grubbs, I I T Research Inst., *10 W. 35th St., Chicago, Illinois*, 60616, United States of America

This project is designed to determine if the extracts and/or particles present in diesel fuel emissions possess carcinogenic or cocarcinogenic activity relative to the pulmonary epithelium. In addition the results should indicate the relative potency of these compounds by comparing their carcinogenicity to that of other materials of known epidemiologic significance (roofing tar, coke oven extract and cigarette smoke condensate). The investigators will utilize the intratracheal instillation method of Saffiotti for the administration of the test substances. A whole animal model will be used. The dose-range study on diesel particles and diesel particle-Fe2O3 mixtures has been evaluated from a toxicity standpoint. None of the experimental treatments appeared to affect mortality during treatment or the 5-week recovery period nor final weight of the hamsters. Animals in high dose test groups lost small amounts of weight in the first 2-3 weeks, then recovered and gained weight comparable to control groups. Nonrespiratory tract pathology in diesel particle groups was not significant. Trachea and lungs in treated animals showed a variety of responses including hyperplasia, metaplasia, adenomatoid lesions, and early adenoma. These changes were more severe than in their respective control groups. The dose-range study of the three extracts (diesel exhaust, coke oven and roofing tar) and of cigarette smoke condensate is in progress. Effects on mortality and weight gain will be evaluated during the next quarter.

431. ONCOGENICITY RELEVANT BIOCHEMICAL EVALUATIONS IN ANIMALS EXPOSED TO DIESEL EXHAUST

Danner, R., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio*, 45268, United States of America

OBJECTIVES: The objectives of this study are to (1) determine the degree of enzyme induction resulting from the presence of aromatic hydrocarbons in diesel exhaust, and (2) evaluate the influence of diesel exhaust exposure upon the distribution of benz(alpha)pyrene (BaP) in the body.

APPROACH: Groups of Strain A mice will be exposed for 3, 4, and 9 months to diesel exhaust. Following completion of exposure, cytochrome P450 and aryl hydrocarbon hydroxylase (AHH) levels will be measured in a portion of the animals. Subgroups will be instilled with 3HBaP followed by BaP analysis of liver, lung, and testes after 2, 24 or 168 hours.

432. LUNG TUMOR INDUCTION BY DIESEL EXHAUST IN STRAIN 'A' MICE

Orthoefer, J. G., Pepelko, W. E., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio*, 45268, United States of America

OBJECTIVE: The objective of this study is to assess the induction of tumors in strain 'A' mice following inhalation exposure to either whole diesel exhaust emission, or components of exhaust. The strain 'A' mouse model is used because of sensitivity to induction of lung tumors, small size allowing exposure of large numbers, and the relatively short time required for tumor induction.

APPROACH: Groups of mice are exposed from weaning age until 9 months old to the experimental conditions. Exposures are via inhalation 8 hours/day, 5 or 7 days/wk. Groups of 60 females each were exposed to diesel exhaust, urethane or both in combination. Two groups of 400 males each were exposed to diesel exhaust or clean air. Studies are being planned for FY 80 to expose mice to B(a)P, carbon particulate or carbon particulate plus B(a)P.

PROGRESS: Exposure of female mice to diesel exhaust resulted in a significant increase in tumor incidence. Information for males is to be available December 1979.

433. INHALANT ONCOGENICITY OF DIESEL EXHAUST USING SYRIAN GOLDEN HAMSTERS

Orthoefer, J. G., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio*, 45268, United States of America

OBJECTIVE: The objective of this study is to evaluate the effects of long-term exposure to diesel exhaust emissions via inhalation upon lung tumor induction.

APPROACH: Two groups of 100 female Syrian hamsters will be exposed for 20 months to either clean, filtered air or diesel exhaust. Following completion of exposure the animals will be sacrificed and the lungs preserved and examined for tumors.

PROGRESS: None. Exposures are continuing.

434. COMPARISON OF CARCINOGENIC POTENCY OF DIESEL EXHAUST PARTICULATE, COKE OVEN EMISSIONS, CIGARETTE SMOKE CONDENSATE AND ROOFING TAR

Orthoefer, J. G., U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab., *5555 Ridge Ave., Cincinnati, Ohio*, 45268, United States of America

OBJECTIVE: The purpose of this study is to compare the relative carcinogenic potency of diesel exhaust, coke oven emissions, cigarette smoke condensate and roofing tar. Since there is some epidemiological data for the last 3 pollutants, particularly coke oven emissions, the relative potency of diesel exhaust in humans can then be estimated.

APPROACH: An initial study will be conducted to determine the maximum tolerated intraperitoneal doses. Following this 50 animals/group will be injected intraperitoneally 3 times per week for 24 weeks with the maximum tolerated dose of one of the 4 pollutants. The animals will be sacrificed at 9 months of age and examined for lung and other tumors.

435. ASSESS ONCOGENIC, REPRODUCTIVE AND GENERAL TOXICITY IN STRAIN 'A' MICE EXPOSED IN MULTIPLE GENERATIONS TO DIESEL EXHAUST

Briggs, G. B., Henne, S., WIL Research Lab., *3154 Exon Ave., Cincinnati, Ohio*, 45241, United States of America

OBJECTIVES: (1) To evaluate the influence of diesel exhaust exposure upon reproductive parameters; (2) to determine

if diesel exhaust exposure causes an increase in tumorigenesis in F1 generation offspring born and raised under the experimental conditions.

APPROACH: Four groups of 20 female Strain 'A' mice will be exposed to either clean air or diesel exhaust. Groups of males will receive similar exposure. At sexual maturity the animals will be bred according to the following design. Clean air F x clean air M, clean air F x Diesel M, Diesel F x clean air M, Diesel F x Diesel M. F1 animals will be bred at maturity to produce an F2 generation. End points include reproductive parameters and incidence of lung tumors.

436. ASSESSMENT OF ONCOGENIC POTENTIAL OF DIESEL EXHAUST

Shinozuka, H., Lombardi, B., University of Pittsburgh, School of Medicine, Dept. of Pathology, *3550 Terrace St., Pittsburgh, Pennsylvania*, 15261, United States of America

OBJECTIVE: The objective of this study is to determine if exposure to diesel exhaust results in liver cancer using a rapid sensitive in vivo test.

APPROACH: Sensitivity of lung tissues in rats to induction will be measured by partial hepatectomy to stimulate cell division and feeding of a choline deficient diet which acts as a tumor promotor. Following a three-month exposure to diesel exhaust the livers will be examined for islands of transformed cells by staining for gamma glutamyl transferase. If islands are found the remaining animals will be sacrificed after a six-month exposure and examined for liver tumors. If no islands are found the remaining animals will be exposed for at least one year.

PROGRESS: The three-month exposures have been completed and livers are being evaluated for islands.

437. CHEMICAL CHARACTERIZATION AND TOXICOLOGIC EVALUATION OF AIRBORNE MIXTURES

Dalbey, W. E., Oak Ridge National Lab., *P.O. Box Y, Oak Ridge, Tennessee*, 37830, United States of America

OBJECTIVE: Comprehensive definition of the toxicologic effects of the Army diesel fuel smoke system; to establish an in vitro mutagenicity screening battery and to evaluate three short-term in vivo systems for prediction of oncogenic potential.

Rodents will be exposed to aerosols of diesel fuel smoke in whole-body, dynamic flow exposure chambers. The three phases of the study include determination of LC50 and LCT50, biologic effects of various intermittent repeated exposure regimens, and selection of exposure regimens for 13 wk studies. Three in vitro tests - bacteria, yeast and hamster cell culture - will be evaluated for ability to predict mutagenicity of colored smoke components and munition compounds. Shorter-term in vivo systems - development of skin papillomas in Sencar mouse and lung adenomas in two strains of mice - will be evaluated for their sensitivity in prediction of oncogenic potential of munition compounds.

438. HEALTH EFFECTS OF SYNFUELS

Renne, R. A., U.S. Dept. of Energy, Battelle Pacific Northwest Lab., *P.O. Box 999, Richland, Washington*, 99352, United States of America

This research project examines the carcinogenic potential of various materials and chemical fractions from the solvent-refined coal process, on a comparative basis, with materials from other synthetic fossil-fuel technologies, crude petroleum, and pure samples of known carcinogens. The animal model being utilized is the mouse skin-painting assay, a system which has been used extensively in the past to assay the carcinogenicity of polycyclic-aromatic-hydrocarbon-containing fossil fuels and fuel derivatives. This research is being correlated with ongoing mutagenesis studies of the same materials in an attempt to determine the correlation between mutagenesis and carcinogenesis data for fossil-fuel materials and their chemical fractions.

439. COAL LIQUIDS CARCINOGENICITY SCREENING TESTS

Calkin, W. H., E.I. du Pont de Nemours & Co. Inc., *P.O. Box A, Aiken, South Carolina*, 29801, United States of America

The summary for this project is under entry no. 385.

440. INSULATING MATERIALS, LONG-TERM INHALATION EFFECTS - EPA

Moorman, W., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Biomedical & Behavioral Science, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Chronic biologic effects following long-term inhalation of fibrous glass used in insulating trades will be studied by contract. Specific objectives include: (1) the evaluation of carcinogenic risk; (2) the evaluation of the fibrogenic potential; and (3) the character of pulmonary responses, both physiological and pathological (including deposition patterns). The results from this effort will be useful in evaluating the validity of the federal standard.

These objectives were identified as research gaps in the 1974 NIOSH-sponsored symposium (Occupational Exposure to Fibrous Glass - HEW Publication No. NIOSH 76-151) on fibrous glass and the 1977 NIOSH Criteria Document for Fibrous Glass. The increased usage, along with epidemiological and experimental data, emphasizes the need for such long-term investigation.

It is estimated that 200,000 workers (insulation installers, manufacturing personnel, and laminate construction workers) are exposed annually. Past accomplishments include: contract award to Battelle Columbus Labs (Contract No. 210-78-0037); development of the fibrous aerosol technology; and initiation of inhalation exposures. Receipt of the final contract report is scheduled for July 1981.

441. INSULATION - CARCINOGENIC AND FIBROGENIC MATERIALS

Pickrell, J. A., Lovelace Center for the Health Sciences, *5200 Gibson Blvd. S.E., Albuquerque, New Mexico*, 87108, United States of America

Conservation of energy is an important part of our national energy policy. Implementing this policy will require increased use of insulating materials including fibers of glass, rock wool and ceramic materials. Our current knowledge of the fibrogenic and carcinogenic properties of these materials and binders used in their commercial application is inadequate considering their increasingly widespread utilization. Potential insulation material toxicants are being inventoried and assigned priority for study in multi-tiered toxicological tests. High priority is assigned to studies of phenol formaldehyde resin binder and glass fibers. In vitro cytotoxicity tests will be performed with alveolar macrophages and type II epithelial cells. Inhalation studies with binder and fibers in varying sizes and concentrations will be conducted in rodents. These will be used to establish deposition and retention patterns as a prelude to evaluating health effects. Serial sacrifice studies are planned to define morphologic changes. Biochemical changes will define indicators of early damage and correlate them to in vitro studies. Biochemical indicators of connective tissue changes will be correlated to development of fibrosis and neoplasia. The studies will be used to define potential lifespan toxicity studies. If necessary for extrapolation of data to man, limited studies will be conducted in non-rodent species.

442. INSULATING MATERIALS - LONG-TERM INHALATION EFFECTS

Mitchell, R. I., Battelle Memorial Inst., Columbus Laboratories, *505 King Ave., Columbus, Ohio*, 43201, United States of America

With the increased emphasis on energy conservation, there has been an increase in the usage of fibrous glass products for thermal insulation. This has led to an increase in the exposure both environmentally as well as occupationally. Animal tests in which glass fibers have been introduced into the pleura of rats have shown that, depending upon the size of the glass fibers, a moderately high incidence of mesotheliomas can be produced. Similar tests with asbestos have produced a higher percentage of mesotheliomas. The objective of the program is to conduct a long-term, low-level inhalation study of glass fibers of known size in order to determine the adequacy of current OSHA standards.

443. INHALATION HAZARDS TO URANIUM MINERS

Cross, F. T., U.S. Dept. of Energy, Battelle Pacific Northwest Lab., *P.O. Box 999, Richland, Washington*, 99352, United States of America

This project, in which both large and small experimental animals are used to model human respiratory system disease, is concerned with determining the specific biological effects of chronic exposure to known levels of pathogenic uranium mine air contaminants. We are attempting to identify the agents (or combinations of agents, both chemical and radiological), and the exposure levels, that result in respiratory tract lesions, including respiratory epithelial carcinoma, pneumoconiosis, pulmonary fibrosis and emphysema.

444. POSTAL CANCELLATION INK

Plotnick, H., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Biomedical & Behavioral Science, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

This project represents the continuation of a combined in-house and contract effort begun in FY 79. The purpose of the project is to assess the safety of a new cancellation ink at the request of the U.S. Postal Service. The in-house efforts involved assessment of skin irritancy, skin sensitization, and ocular irritancy, and were completed during FY 79. The contract effort, a skin painting carcinogenesis bioassay in mice, began in June 1979, and will be completed early in FY 81. The contractor is Borriston Research Laboratories, Temple Hills, Maryland (Contract No. 210-79-0035).

The U.S. Postal Service estimates that 2000 workers are exposed to the ink during the filling and cleaning of automatic mail cancellation machinery.

445. INVESTIGATION OF THE CARCINOGENIC ACTION OF METALLIC AND MINERAL PARTICULATES IN THE LUNG BY INTRABRONCHIAL PELLET IMPLANTATION

Levy, L. S., Martin, P. A., University of Aston in Birmingham, Dept. of Safety & Hygiene, *Gosta Green, Birmingham B4 7ET, England, United Kingdom*

OBJECTIVE: To investigate the possible causation of human lung cancer in both occupationally and non-occupationally exposed populations by airborne industrial and environmental contaminants.

APPROACH: This study proposes to explore the effect of low levels of putative carcinogens on the rat lung, both alone and in conjunction with other materials introduced by a variety of routes. The technique is non-inhalational and a further adjunct of this study is to examine critically the role and feasibility of such non-inhalational techniques in the identification of potential industrial and environmental lung carcinogens.

PROGRESS: In the process of setting up the study.

446. DETERMINATION OF THE CHRONIC MAMMALIAN TOXICOLOGICAL EFFECTS OF RDX (TMP064)

Lish, P. M., I I T Research Inst., *10 W. 35th St., Chicago, Illinois*, 60616, United States of America

OBJECTIVE: To determine the mammalian chronic toxicity and carcinogenicity of RDX to provide for the development of a portion of the data base to assess the hazard associated with discharged of RDX to the environment from Army-owned ammunition plants.

Studies will be performed to determine the chemical-biological interaction of RDX for chronic exposures to mammals. This will include assessment for carcinogenicity.

447. APPLICATION OF SKIN TEST AS A TOOL IN TESTING POLLUTANTS FOR CANCER

Jagannatha Rao, K. S., Sri Venkateswara University, Inst. of Environmental Studies, Dept. of Zoology, *Tirupati 517502, AP, India*

We are planning a wide survey of many man-made substances like pesticides, few heavy metals, factory effluents, for carcinogenic properties, using skin as a simple testing tool because of its early response to these materials and certain advantages in histopathological studies. We are also planning to test certain substances as anticancer drugs using DNA dependent RNA and DNA polymerase enzyme activities as indicators of the anticancer drug action. This study will help in early screening of many pollutants for their carcinogenic properties and of certain substances for their anticancer action.

448. ENVIRONMENTAL DUSTS AND MACROPHAGE ACTIVATION

Hamilton, J. A., Sloan Kettering Inst. for Cancer Research, *410 E. 68th St., New York, New York*, 10021, United States of America

It has recently become apparent that the environmental component of cancer is more significant that generally imagined. We propose to test noxious dusts and fibers, which are commonly found in the environment, for their ability to induce putative inflammatory mediators from mouse peritoneal macrophages. These molecules are the enzymes, plasminogen activator and collagenase, and prostaglandins. Several environmentally important materials will be used, with particular emphasis on asbestos. These fibers will be manipulated and physical measurements made to determine what structural and chemical characteristics are important for activity in our in vivo and in vitro test systems. We intend to study cellular control mechanisms for the synthesis of the mediators and hopefully to find drugs which could alleviate the deleterious effects of such fibers and dusts. We hope that our data may aid in the establishment of realistic control methods and standards for asbestos levels and types, as we will be placing emphasis on short asbestos fibers. It is also possible that our assays may be useful for detecting other harmful fibers and dusts in the environment. Because peritoneal mesotheliomas are a common form of mesothelioma in asbestos workers, we believe it relevant to be studying the interaction of asbestos with peritoneal cells.

449. HEMATOPOIETIC TOXICOLOGY OF ENVIRONMENTAL POLLUTANTS

Gurney, C. W., University of Chicago, Pritzker School of Medicine, Dept. of Medicine, *5801 S. Ellis Ave., Chicago, Illinois*, 60637, United States of America

We propose to produce and measure subtle degrees of damage to the hematopoietic system with small doses of known hematopoietic toxins, and then carry this approach over to the study of small doses of irradiation or environmental pollutants, in the dose range not generally considered to be harmful to the blood-forming system. This necessitates use of an in vivo mouse model in which the hematopoietic reserve has been removed by administration of 89Sr followed by splenectomy.

Once we have established and recorded the impairment of one or more components of hematopoiesis, we will investigate the degree to which repeated exposures, or combinations of several different agents, may be cumulative. In addition to studying damage to the primitive precursor cell compartments, we will be searching for and attempting to establish methods for assessing damage to the stroma or hematopoietic microenvironment.

Finally, a long-term objective is to determine whether one or a series of very small insults to the bone marrow and its microenvironment by various pollutants or hematopoietic toxins may contribute to leukemogenesis.

BIBLIOGRAPHIC REFERENCES: Large, Sustained Oscillations of Reticulocyte and Hematocrit Levels in W/W2 Mice Following 89Sr. C.W. Gurney, E. Simmons, and E.O. Gaston. (Abs) Experimental Hematology 8: No. 7, 239, 1980.

450. SKIN AND PULMONARY CARCINOGENESIS

O'Connor, T., U.S. Dept. of Energy, Argonne National Lab., *9700 S. Cass Ave., Argonne, Illinois*, 60439, United States of America

This program has three segments concerned with: (1) enzymatic metabolism of chemical carcinogens; (2) the mechanism of skin carcinogenesis and the factors that determine susceptibility to cancer induction and co-carcinogenic effects; and (3) the critical examination of the use of mouse lung tumors as a test system for the assessment of environmental pollutants for tumorigenic potential. The three segments are interrelated and are concerned with two tissues that are continuously exposed to environmental factors, namely, lung and skin. The studies examine the enzymatic production of the ultimate carcinogen, the relationship of specific DNA damage to subsequent cancer production, and the factors that influence the expression of the cancer-producing changes. An understanding of the factors that may influence susceptibility, such as age, proliferative activity, hydroxylase activity, and infection, are of importance for the assessment of risk and are studied in the rodent lung. Because of

the problems in extrapolation of animal data to estimates of risk in man we are attempting to carry out some studies on human skin.

451. ENVIRONMENTAL CARCINOGENESIS AND BIOASSAY - SKIN

Cavalieri, E. L., University of Nebraska, Medical Center, School of Medicine, Eppley Inst. for Cancer & Allied Diseases, *42nd & Dewey Aves., Omaha, Nebraska*, 68105, United States of America

No summary has been provided to the Smithsonian Science Information Exchange.

452. EVALUATION OF A SHORT-TERM IN VIVO SYSTEM FOR RISK ASSESSMENT OF ENVIRONMENTAL CHEMICALS

Couri, D., Ohio State University, Columbus Campus, School of Medicine, Dept. of Pharmacology, *370 W. 9th Ave., Columbus, Ohio*, 43212, United States of America

OBJECTIVE: The Cooperative Agreement will attempt to validate the short-term in vivo system that has been proposed by HERL-Cincinnati for assessing the carcinogen risk to man posed by environmental chemicals. This will require the validation of hemoglobin alkylation as a dose monitor for human exposure to carcinogens.

APPROACH: The system consists of 3 components: 1) whole animal and human monitoring of exposure as measured by hemoglobin alkylation, 2) target organ dose as measured by DNA binding and 3) carcinogenic potency measured by the rat liver altered-enzyme assay. The investigator will test a chemical class of carcinogens in the system in order to determine whether the responses in the 3 components correlate. The investigator will also determine the hemoglobin binding in humans of an environmental carcinogen as part of their evaluation of the usefulness of hemoglobin alkylation as a dose monitor.

453. AN ECOLOGICAL APPROACH TO ENVIRONMENTAL CANCER

Sonstegard, R. A., McMaster University, Dept. of Biology-Pathology, *1200 Main St. W., Hamilton, Ontario*, L8S 4L8, Canada

OBJECTIVE: Development of a system of monitoring tumor frequencies in feral fishes as a sentinel for the detection of environmental carcinogens. Initiate cohort epidemiological studies of 'heavy' fish-eaters in the Great Lakes basin.

APPROACH: Field epizootiological studies of fishes in the Great Lakes basin strongly link elevated tumor frequencies with extrinsic factors, possibly pollutants. Sports fishermen consume these fish(es) in quantity, and in light of their high xenobiotic burdens (they are banned from commercial sale), this represents an uncontrolled source of carcinogen exposure. In light of the same, feeding trials (feeding diets of fish which exhibit pathobiological response(s) which epizootiological studies link to extrinsic factors to laboratory rats and fishes) are being made with particular reference to health effects associated with dietary consumption of fish. The health responses recorded in these feeding trials will be incorporated (e.g., clinical chemistry) into the cohort epidemiological studies of heavy fish-eaters.

454. DEVELOPMENT OF A TISSUE SELECTIVE IN VIVO BIOASSAY FOR ENVIRONMENTAL AGENTS PRODUCING DNA DAMAGE

Koestner, A., Ohio Agricultural Research & Development Center, *Columbus, Ohio*, 43216, United States of America

OBJECTIVE: Integrate selected in vitro assay procedures into the animal model system in order to develop a rapid, inexpensive in vivo bioassay system that will permit a quantitative, tissue specific prediction of the carcinogenic potential of environmental agents alone and in combinati n with one another.

APPROACH: Micropunch tissue biopsies will be removed, the cellular matrix dispersed, and DNA assayed by use of sucrose gradients or agarose gels. The detection of DNA following separation by molecular weight will involve the use of a spectrofluorometric assay permitting analysis of DNA concentrations in the nanogram range.

455. THE MARSUPIAL NEONATE AS A MODEL FOR THE IDENTIFICATION AND EVALUATION OF ENVIRONMENTAL TOXICANTS

Jurgelski, W., Hudson, P. M., Falk, H. L., Zimmerman, L. E., Henry, J. M., Palmer, N., Hoffman, S., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Environmental Health Sciences, Office of Health Hazard Assessment, *P.O. Box 12233, Research Triangle Park, North Carolina*, 27709, United States of America

This project seeks to develop the opossum Didelphis virginiana as a biomedical model by (1) characterizing the normal neonatal and developing opossum anatomically and physiologically and (2) determining the pathophysiologic response of these animals to selected environmental toxins and carcinogens.

BIBLIOGRAPHIC REFERENCES: Jurgelski, W. Jr. The Marsupial as a Laboratory Animal. ILAR News, Institute of Laboratory Animal Resources, National Academy of Sciences, 22: 18-21, 1979.

V. REGISTRIES OF OCCUPATIONAL AND ENVIRONMENTAL CARCINOGENESIS

456. MORTALITY-MORBIDITY STUDY AND TUMOR REGISTRY FOR PETROLEUM, REFINING, PETROCHEMICAL AND RESEARCH AND DEVELOPMENT WORKERS

Weaver, N. K., Schottenfeld, D., American Petroleum Inst., Dept. of Medicine & Biological Science, *2101 L St. N.W., Washington, District of Columbia*, 20037, United States of America

The objective of this study is to conduct a comprehensive prospective epidemiological investigation among petroleum industry workers as a means of determining possible health consequences of occupational exposure. A data gathering, reporting, and interpreting system appropriate for the conduct of a continuing epidemiological study will be established. Patterns of morbidity (illness), mortality and tumor occurrence will be identified and compared with the rates for a suitable control population. Relationships between morbidity and mortality patterns will be related to occupational characteristics, and trends in affected worker populations will be defined. The data received from participants will be analyzed and interim reports to each individual company on its own material made. The project will encompass all disease categories in the International Classification of Diseases and the morbidity portion of the study will be based on all sickness absences of five or more days' duration.

457. REGISTER OF WORKERS OCCUPATIONALLY EXPOSED TO TRICHLOROETHYLENE

Tola, S. A., Korkala, M. L., Inst. of Occupational Health, Dept. of Epidemiology & Biometry, *Haartmaninkatu 1, SF00290 Helsinki 29, Finland*

A cohort of 1,881 workers has been identified from the list of workers whose urinary trichloroacetic acid has been measured at the Institute of Occupational Health. The cancer mortality of this group will be studied. Since most of the workers are relatively young (70% less than 50 years old), a prospective follow-up study will be undertaken after registering the exposure level and current vital status of the workers. The data will be analyzed by comparing the observed cancer mortality rates to those expected, as calculated from the national figures. It is also possible to compare the mortality figures with those of other occupational cohorts which are registered at the Institute of Occupational Health (e.g., stone workers, foundry workers, workers exposed to styrene).

458. MESOTHELIOMA REGISTER

Planteydt, H. T., Pathologisch Anatomisch Laboratorium, *Noordpoortplein 2, Middelburg, Netherlands*

In order to obtain information about the frequency of mesothelioma of pleura, peritoneum and pericardium, from 1969 onwards, all pathologists in the Netherlands were asked to cooperate in the registration of all histologically verified cases. These results are compared with the data of the Central Bureau of Statistics. In many cases slides and/or tissues were available: in a limited number of cases, electron microscopical investigations of lung tissue were done for asbestos. The occupational

history was investigated extensively. Many cases are reviewed by a mesothelioma committee (Planteydet, de Jagar, van der Schoot). The geographical distribution, relation to occupational history and exposure to asbestos are recorded in several ways. From 1976 onwards registration, together with the other investigations, follows the same lines as the mesothelioma register in the United Kingdom. Since 1976 collaboration with other mesothelioma registers in the EEC has been established.

459. FRENCH MESOTHELIOMA REGISTER

Bignon, J., Perdrizet, S., Di Menza, L., Sebastien, P., Nebut, M., Centre Hospitalier Intercommunal de Creteil, Service Hospitalier Universitaire de Pneumologie, *40 Ave. de Verdun, 94010 Creteil, France*

To date 197 proved cases of mesothelioma (mainly pleural) have been reported for the period 1965-1978, a moderate increase over time being noted. Occupational and para-occupational asbestos exposure was recorded in 77 percent and 3 percent of registered cases respectively. As the number of cases notified to the register is obviously an underestimate, it is intended to evaluate the annual incidence of this tumour by retrospective registration. Relationships with asbestos exposure and with other pollutants will be sought, and case-control studies for a dose-response relationship with asbestos carried out using retrospective inquiries and measurements of fibres in tissue.

460. CALVADOS CANCER REGISTRY

Robillard, J. M., Abbatucci, J. S., Mace, J., Thouin, A., Centre Regional Francois Baclesse, Service de Statistiques, *Rte. de Lion-sur-Mer, 14018 Caen, France*

The registry compares cancer morbidity in the Department of Calvados with that in the French regions of Bas-Rhin and Doubs, in other regions bordering France (Geneva, Lausanne, Neuchatel, Saragossa) and in more distant parts (Warsaw, Connecticut, Cuba, southern England, etc.). Morbidity time trends are estimated and compared with those observed in other registries. The geographical distribution of cancer within Calvados is examined to study possible etiological factors (e.g. predominance of lung cancer in areas with asbestos industries). The Registry records cancer cases in the Department as accurately as possible and assists with the planning of screening and prevention in Lower Normandy.

461. REGISTRATION OF DIOXIN WORKERS

Halperin, W., Lemen, R., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio*, 45226, United States of America

Tetrachlorodibenzo-p-dioxin (TCDD) is a highly toxic contaminant of manufacturing processes which use trichlorophenol as a feedstock. The manufacture of the herbicide 2,4,5-T is an example. TCDD is a chloracnegen and acute toxin as well as a carcinogen and a teratogen in laboratory animals. In its use as a defoliant, large numbers of people have been exposed.

We propose establishing a registry of workers who have been exposed to TCDD during manufacture of TCP and other compounds. This registry may serve as a base for cohort mortality studies and for possible studies of reproductive effects and morbidity.

462. THE SWEDISH CANCER ENVIRONMENT REGISTRY

Wiklund, K., Einhorn, J., National Board of Health & Welfare, Planning Div., Dept. of Statistics, *Linnegatan 87, 10630 Stockholm, Sweden*

The persons with tumours who are entered in the Swedish Cancer Environment Registry are those contained in the Swedish Cancer Registry for a period 1961-1973 and verified as being registered in the 1960 Population and Housing Census. During the period from 1 January 1961 to 31 December 1973, the number of cases of cancer at sites 140-205 in the Registry was 376,015. Individuals were identified by their personal identification number. On linking the files one per cent of entries in the Cancer Registry could not be traced. The information entered in the Registry, obtained from the 1960 Population and Housing Census, concerned the following: occupation, main occupation during the year, economic activity, occupational status, gainful employment, county, municipality or parish, location of place of work (county, municipality, parish), country of birth and education.

463. THE SWEDISH TWIN REGISTRY STUDIES

Friberg, L. T., Cederloef, R., Lundman, T., Floderus Myrhed, B., Karolinska Institutet, Dept. of Environmental Hygiene, *Solnavagen 1, Box 60400, S10401 Stockholm 60, Sweden*

In 1961 the Twin Registry covered about 10,000 same-sexed pairs born during the period 1886-1925. The registry was expanded in 1973 to include about 15,000 pairs born in 1926-1958. The aim of the Twin Registry is to study influences of the environment on morbidity and mortality, including cancer morbidity and mortality, based on periodical matching with the Swedish Cancer Registry. The latest updating was performed during 1979. The mortality data are evaluated through a continuous follow-up of mortality within the registries. The total twin program was reported in Acta Medica Scandinavia, Suppl. 612, 1977, in 'The Interactions of Smoking, Environment and Heredity and their Implications for Disease Etiology.' The latest report concerning cancer by Cederloef-Floderus, 'Cancer Mortality and Morbidity among 23,000 Unselected Twin Pairs' (1979) dealt mainly with concordance rates for cancer of all sites and cervical cancers.

464. VALIDITY AND UTILITY OF OCCUPATIONAL DATA IN A POPULATION-BASED CANCER REGISTRY

Swanson, G. M., Michigan Cancer Foundation, Dept. of Biometry & Medical Sociology, *110 E. Warren Ave., Detroit, Michigan*, 48201, United States of America

Approximately 1,200 cases are being reviewed to determine the validity and utility of occupational data obtained from hospital records by the Michigan Cancer Foundation Registry. Routinely recorded data are being compared with data obtained from interviews and from industrial listings to evaluate validity. Methods for routinely selecting occupations that appear to be at excess risk for cancer from these data will be developed after completion of the validity study.

VI. DIAGNOSTIC AND PATHOLOGICAL STUDIES OF OCCUPATIONAL AND ENVIRONMENTAL CANCER

465. STUDIES OF NASAL CANCER IN WORKERS EXPOSED TO NICKEL AND DEVELOPMENT OF METHODS FOR SCREENING AND EARLY DIAGNOSIS (ABBREV)

Boysen, M. E., Reith, A. K., Norsk Hydro's Inst. for Cancer Research, Laboratory of Electron Microscopy, *Montebello, Oslo 3, Norway*

OBJECTIVE: Histopathological follow-up study of known cases and screening for new cases of precancerous lesions by light microscopy (LM). Characterization of normal, metaplastic, dysplastic (precancerous) and cancerous lesions of the nasal mucosa by means of scanning and transmission electron microscopy (SEM, TEM), morphometry, autoradiography (cell kinetics), and development of cytological screening methods for cancerous and precancerous lesions and an experimental model using rats for upper airway carcinogenesis.

APPROACH: Biopsies from the nasal mucosa of workers in a nickel refinery were plastic-embedded for histopathology and morphometry. A method was introduced for characterization of large mucosal areas by SEM and, thereafter, areas of interest were sectioned for comparison with LM and TEM. Cytological samples from the regions adjacent to the biopsy were taken with a special brush. A new model was developed for morphometric characterization of the different histopathological stages of nasal mucosa.

We will now develop an experimental model with rats for inhalation and installation of carcinogens to be used for comparison with the pathological alterations seen in human nasal mucosa. Furthermore, cytokinetic evaluation will be made by in vitro incubation in tritiated thymidine.

PROGRESS: The histopathological follow-up study has shown a marked decrease in the number of cases with dysplasia, probably as a consequence of the environmental conditions in

the refinery in recent years. Our morphometric studies show that different histopathological stages can be characterized objectively (Pathology: Research and Practice, in press). The SEM studies have shown that the different stages are also reflected in different surface structures of cells at the luminal site.

466. NASAL CARCINOMA IN NICKEL WORKERS

Torjussen, W., Solberg, L. A., Haug, F. M., Central County Hospital Vest Agder, Dept. of Otolaryngology, *4601 Kristiansand, Norway*

The objective of the investigation is to study the influence of occupational nickel exposure on the nasal mucosa and body fluids. Plasma, urine and standardized biopsy specimens from the nasal mucosa from 318 nickel workers, 15 retired nickel workers and 57 controls were analyzed for nickel by atomic absorption spectrometry. The biopsy specimens were also graded histologically to reveal precancerous and cancerous changes by applying light and electron microscopical examinations. Histochemical methods were applied to localize the metal within the tissue. A clinical evaluation by rhinoscopy was used to grade the macroscopic changes of the nasal mucosa. Smoking habits and amounts smoked, duration of nickel exposure, type and amounts of airborne nickel exposure and age were evaluated. Multiple regression analysis was performed to explain the histopathological changes and the rhinoscopical findings by independent variables such as nickel exposure, smoking habits, concentrations of nickel in plasma, urine and nasal mucosa, working categories and age.

467. IMMUNOLOGICAL CRITERIA IN THE DETECTION OF HIGH OCCUPATIONAL CANCER RISK AMONG TEXTILE WORKERS

Korosteleva, T. A., Belokhvostova, A. T., Movsesjan, K. S., Kuznetsov, S. I., N.N. Petrov Inst. of Oncology Research, Laboratory of Experimental & Clinical Oncoimmunology, *Leningradskaja St. 68, Pesochny 2, Leningrad 188646, Russia, Union of Soviet Soc. Republics*

The purpose is to examine textile workers handling direct dyes containing benzidine and beta-naphthylamine. The workers have been divided into 3 groups according to extent and duration of exposure. The following immunological tests have been used: (1) determination of benzidine as haptene in the blood serum of workers, splitting of the direct dyes by specific rabbit immune serum; (2) determination of an endogenous carcinogen, the metabolite of tryptophane-3-hydroxyanthranilic acid (3HAA), using specific rabbit immune serum in immune diffusion in agarose as a criterion of disturbances in tryptophane metabolism. Such disturbances have frequently been observed in patients with cancer of the urinary bladder and some other sites (breast, lung); (3) determination of the index of phagocytic activity of blood neutrophils as related to specific and non-specific factors. Particles of activated carbon, loaded by benzidine- and 3-HAA -azoproteins, were used as specific factors, and staphylococcus aureus as a non-specific factor; (4) determination of blast transformation of peripheral leucocytes to PHA and benzidine- and 3-HAA-azoproteins. The blood of non-exposed workers and healthy donors was used as a control.

468. THE CYTOLOGICAL DIAGNOSIS OF BLADDER TUMORS IN DYESTUFF WORKERS

Ishizu, S., Tokyo Women's Medical College, Dept. of Public Health, *10 Kawadacho Shinjuku-Ku, Tokyo 162, Tokyo, Japan*

The production and use of benzidine and beta-naphthylamine in the dye industry of Japan were prohibited by law in 1971. However, there are still 4,037 workmen (including retired men) who have been exposed to carcinogenic amines, and risk developing a bladder tumor in the future. This study aims to perform continuous follow-up urine examination of the workers. For the early detection of bladder tumors, routine cystoscopy was considered to be quite unsuitable. The Papanicolaou smear technique of urine examination was introduced into the dye industry of Japan in 1961. A total of 4,037 men were screened first by wet smear and then by Papanicolaou smear. During the 22 years from 1955 to 1977, 192 cases of occupational bladder tumor were discovered; 15 out of 108 men with positive Papanicolaou smears have shown no tumors on cystoscopy; 7 men with negative Papanicolaou smears showed bladder tumors on cystoscopy (false negative); 47 out of 137 men with suspicious Papanicolaou smears had bladder tumors. Seventeen specimens obtained from the occupational bladder tumor patients were histopathologically examined. Of these 17 specimens, 8 showed papillary cancer type, 6 showed an inverted proliferating tumor, and 3 were carcinoma in situ. This study continues.

469. RESEARCH TECHNIQUES AND METHODS FOR DETECTION AND PREVENTION OF CARCINOGENESIS IN INDUSTRIAL WORKERS - A MULTIDISCIPLINARY APPROACH

Tamburro, C. H., Wong, J. L., Kupchella, C. E., University of Louisville, School of Medicine, Dept. of Community Health, *101 W. Chestnut, Louisville, Kentucky,* 40202, United States of America

OBJECTIVES: The multidisciplinary research program goals of this group are to identify and characterize both the toxicity and potential carcinogenicity of vinyl commodity chemicals, to identify how they are handled biologically and to test detection and screening techniques for toxicity in an actual industrial environment.

APPROACH: The individual titles and coinvestigators are as follows: A) Immunological Systems for the Detection of Vinyl Chloride and Other Chemical Injury. H.P. Fortwengler and C.H. Tamburro. B) Biochemical Enzymatic Systems for the Detection of Vinyl Chloride and Other Chemical Injury as a Potential Means of Detection of Cancer in Humans. J.T. Du and C.H. Tamburro. C) Tissue and Urinary Glycosaminoglycan Changes Related to Vinyl Chloride Injury: Use and Early Detection and Diagnosis. C.E. Kupchella. D) Electron Microscopic Evaluation of Liver Injury of Chemical Workers. C.H. Tamburro and G.R. Schrodt. E) Multivariant Analysis of Biological End-Products in Vinyl Chloride Metabolite Synthesis. J.L. Wong and K.G. Taylor. F) Assays for Identification of the Carcinogenic Potential of Industrial Chemicals. U.N. Streips and G. Sonnenfeld. G) Tissue Antigenic Systems for Detection of Chemical Induced Carcinogenesis. E. Espinosa. H) Whole-Body Auto-Radiographic Study of Vinyl Chloride. W.J. Waddell. I) Vinyl Chloride Metabolism in Isolated Liver Cells. R.C. Feldhoff.

470. MORBIDITY AND INDUSTRIAL HYGIENE STUDY OF FIBROUS MINERAL WORKERS (TALC)

Cameron, T., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

A cross-sectional study of 125 mine and mill workers in New York State, who were exposed to talc containing tremolite and anthophyllite, has shown an excess of pleural thickening related to exposure. The workers were given blood tests, chest x-rays, spirometry studies, and respiratory questionnaires.

A cross-sectional medical and industrial hygiene study of talc workers in other states is in progress. This includes 183 workers exposed to Montana talc, 71 workers exposed to Texas talc, and 52 workers exposed to North Carolina talc. The studies are of two types: a cross-sectional prevalence study, and a short-term study of acute pulmonary function changes in some of the workers from the prevalence study.

The prevalence study will examine the association of medical findings with cumulative exposure and respirable particles.

The acute changes in pulmonary function were measured by: 1) chest x-rays; 2) spirometry studies (before and after shift in some workers); 3) diffusion studies in workers older than 35 years of age; 4) sputum tests on workers older than 35 years of age; 5) respiratory questionnaires with respiratory symptoms, smoking, and occupational history information; and 6) personal and area environmental sampling.

471. AHH INDUCIBILITY AND DEVELOPMENT OF BRONCHOGENIC CARCINOMA AND MESOTHELIOMA IN SMOKERS AND NON-SMOKERS EXPOSED TO ASBESTOS (ABBREV)

Simonsson, B. G., Korgsgaard, R., Skerfving, S., Stiksa, G., University Hospital of Lund, Dept. of Lung Medicine/Research, *EB-blocket, S22185 Lund, Sweden*

The aim of the study (begun in 1976) is to elucidate the role of aryl hydrocarbon hydroxylase (AHH) in bronchogenic and pleural carcinogenesis in individuals exposed to asbestos and to examine the possible role of lymphocyte AHH induction

levels in diagnosing individuals at high risk of developing such cancers.

The complete clinical material will comprise about 1000 workers with varying degrees of exposure to asbestos.

Venous blood samples from exposed workers, e.g., insulation workers, have been assessed for AHH inducibility at the Department of Tumour Cytogenetics at the Wallenberg Laboratory in Lund. Further examinations include medical check-ups, extensive occupational and smoking histories, chest X-rays and in some cases sputum cytology and dynamic spirometry.

At present, about 800 workers exposed to asbestos have been examined. Two deaths from mesothelioma and bronchogenic carcinoma have occurred, both in the group of smokers with very high AHH inducibility. This is consistent with previous results from our studies on AHH activity in patients with bronchogenic carcinomas and indicates a statistical association between tobacco consumption, exposure to asbestos and high AHH inducibility in patients developing primary neoplasms of the pleurae or bronchi, i.e. the synergistic effect of smoking and exposure to abestos is further augmented by high enzyme activity.

472. LEUKOCYTE ADHERENCE INHIBITION MEASUREMENTS IN EARLY DETECTION OF CANCER

Sanner, T., Kotlar, H. K., Eker, P., Norsk Hydro's Inst. for Cancer Research, Laboratory for Occupational Cancer & Carcinogenesis, *Montebello, Oslo 3, Norway*

OBJECTIVE: To investigate the possible use of leukocyte adherence inhibition measurements in early detection of cancer and to identify groups at high risk of developing cancer.

APPROACH: The leukocyte adherence inhibition (LAI) test is based on the finding that leukocytes from sensitized persons show a reduced adherence to glass compared to leukocytes from non-sensitized persons when mixed in vitro with the relevant antigen. The published literature indicates that the LAI test possesses a high degree of specificity. Since it may take several years from the time when first cancer cells are formed to the time when a tumor is diagnosed, the possibility exists that specific cell mediated anti-tumor responses may be observed long before any clinical symptoms of the tumor appear. In the present investigation we have concentrated on breast and lung cancer. The LAI response will be measured in persons with untreated breast and lung cancer. Furthermore, measurements will be made on persons with different risk factors for developing these types of cancer, such as women with benign breast diseases, women with breast cancer in the family, smokers and persons working with asbestos.

PROGRESS: Preliminary data indicate that the number of positive LAI responses is considerabely higher in groups of women with breast cancer risk factors than in groups with a non-defined risk factor.

473. ASBESTOS LUNG AND MESOTHELIOMA SURVEY IN THE UNITED KINGDOM

Wagner, J. C., Jones, J. S., Pooley, F. D., Berry, G., Medical Research Council, Pneumoconiosis Unit, Dept. of Pathology, *c/o Llandough Hospital, Penarth CF6 1XW, Wales, United Kingdom*

The aims of this program are to: (1) determine the number of patients dying in 1976 from primary pleural or peritoneal mesothelioma in the United Kingdom, (2) obtain samples of tumor from each autopsy to confirm the diagnosis and determine histological types, (3) examine lung tissue from each autopsy in order to estimate whether asbestos is present and, if present, the amount and type(s), (4) examine control material for the presence of asbestos comprising (a) tumor and lung tissue from the next case of bronchial carcinoma to come to post mortem, of the same sex and within five years of age of the mesothelioma patient(s) and (b) lung tissue from the next case of cerebrovascular accident to come to post mortem, of the same sex and within five years of age of the mesothelioma patient(s), in 1977 samples of lung alleged to be associated with asbestos exposure, from surgical cases of lung cancer and from post mortem cases with pleural plaques seen at two centers.

474. THE APPLICABILITY OF EPIDEMIOLOGIC AND BIOLOGIC MEASUREMENTS FOR THE CONSTRUCTION OF A RISK INDEX FOR ASBESTOS-RELATED DISEASE

Guirgas, H. A., University of California, Irvine Campus, California College of Medicine, *Irvine, California*, 92664, United States of America

There is a recognized increase in cancer of the respiratory and digestive tracts among individuals environmentally exposed to asbestos. In a population likely to be exposed routinely to asbestos, it is desirable to have the most reliable surveillance for early signs of such disease. It is the technical objective of this research task to identify and evaluate reliable and accurately measurable medical markers suitable for routine use in medical surveillance of Navy shipyard workers.

A test group of selected shipyard workers from the Long Beach Naval Shipyard will be thoroughly studied. A control group of workers, from areas in which asbestos exposure is not a hazard, but otherwise comparable, will be used for comparison. The reliability of the following biological markers as indices to susceptibility and as early diagnostic tests will be assessed: inflammatory reactions, changes in immunological status, DNA changes and hematological examinations. The data collected will be subjected to statistical analysis to determine if there are differences between asbestos-exposed and control groups, and to establish the most significant indices of cancer susceptibility.

475. CYTOLOGICAL SCREENING FOR LUNG CANCER USING THE SPUTUM OF WORKERS EXPOSED TO CHROMATES AND ASBESTOS

Melinte, L., Academia de Stiinte Medicale, Inst. of Hygiene & Public Health, Dept. of Occupational Medicine, Cytopathology, *Strada Biserica Amzei 29, Bucharest, Romania*

The aim of the study is to monitor workers at high risk and to estimate the method of cytological screening of sputum for the early discovery of lung cancer as well as of the epithelial disorders which may precede the development of a tumor. Biennial cytological screening of sputum collected for three consecutive mornings and kept in fixative solution was carried out. Paraffin was added and the sputum was dyed with HE, PAS and Pearls. Correlations were made with age, sex, smoking habits, pulmonary antecedents, exposure length, exposure levels and pulmonary radiography. First results show that cytological changes such as bronchial squamous metaplasia are directly proportional to length of exposure and smoking habits.

476. HISTOLOGICAL CLASSIFICATION OF LUNG CANCER IN PERSONS EXPOSED TO ASBESTOS

Auerbach, O., Hammond, E. C., Garfinkel, L., Kaslow, H., Parks, V. R., Conston, A., U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Senior Medical Investigators Laboratory, *Tremont Ave. & S. Centre St., East Orange, New Jersey*, 07019, United States of America

Studies of uranium miners who died of lung cancer have shown a different pattern of histological types from that in non-miners who die of lung cancer. Although there have been some studies of histological type of lung cancer in asbestos workers, these have been on a small series and not classified by the WHO classification of tumor type. Tissue specimens of lung cancer cases (autopsy and surgical specimens) on all subjects diagnosed with lung cancer in a 13 year period are being collected. Asbestos-exposed and non asbestos-exposed persons will be included in this study. Smoking, occupational and residence histories will be obtained from families of the decreased.

477. ASBESTOS-RELATED CHEST DISEASES IN BEDIRLI-YESILOVA-BURDUR

Baris, Y. I., Erkan, L., Hacettepe Universitesi, Faculty of Medicine, Dept. of Chest Diseases, *Ankara, Turkey*

Bedirli is a village with a population of 643, located in southern Turkey, in the region of the lakes. Preliminary mineralogical studies show that there are tremolite type asbestos fibers in the soil and the white stucco used in the village. 200 people (112 males and 88 females) between 25 and 80 years of age were surveyed. The mean age was 44.4. Pleural, diaphragmatic and pericardial calcified plaques were found in 26 percent, 32.9 percent among males and 20.5 percent among females. Pleural thickening was seen in some of the cases with pleural

calcification and in 8 percent of the total population without calcified pleural plaques. This population is being followed to assess risk of mesothelioma and lung cancer.

478. SPUTUM CYTOLOGY AND ASBESTOS EXPOSURE

Simard, A., Band, P., Vauclair, R., Lambert, R., Gibbs, G. W., Saccomanno, G., Feldstein, M., Institut du Cancer de Montreal, Centre Hospitalier Notre Dame, *1560 Sherbrooke St. E., Montreal, Quebec,* H2L 4M1, Canada

An increased risk of lung cancer among asbestos workers has long been known. Sputum cytology in uranium workers led Saccomanno to evaluate mild, moderate, and marked atypia as well as cancer in situ and invasive cancer. Sputum cytology will be related to asbestos exposure in 800 workers. Short (10 years), medium (10-20 years), and long (20 years) exposure will be defined as well as degree of exposure (2 fibres/cc, 2-10). A special group of workers with 35 years of exposure (20-50 fibres/cc) will also be studied. Work histories and other data, namely age, smoking patterns, man-years at risk and years since first exposure, will be put on computer files and related to the severity of atypia.

479. STATISTICAL DATA MANAGEMENT AND COORDINATING CENTER FOR THE TYLER TEXAS ASBESTOS WORKERS PROGRAM

Guinee, V. F., University of Texas, University of Texas System Cancer Center, M.D. Anderson Hospital & Tumor Inst., Dept. of Epidemiology, *6723 Bertner Ave., c/o Texas Medical Ctr., Houston, Texas,* 77030, United States of America

The National Cancer Institute has established a complete medical surveillance program for a group of individuals who were exposed to amosite asbestos fibers in the course of their employment at a pipe insulation manufacturing plant in Tyler, Texas. The surveillance program is a collaborative effort, with the two primary components being the Tyler Asbestos Workers Program (TAWP) affiliated with the University of Texas Health Center at Tyler and the Statistical Data Management and Coordinating Center (SDMCC) directed through the Dept. of Epidemiology, the University of Texas System Cancer Center. The primary goal of TAWP is to make medical and scientific expertise and technology available to the affected workers and to study the pathogenesis and early detection of lung cancer induced by asbestos. The SDMCC is responsible for data collection and analysis of the total program, with particular interest in the epidemiological, laboratory and clinical data produced by TAWP/SDMCC activities.

480. DISCRIMINATION OF OCCUPATIONAL AND NON-OCCUPATIONAL MESOTHELIOMAS INCLUDING ANALYSIS OF DUST PARTICLES AND ASBESTOS IN LUNG (ABBREV)

Otto, H., Pathologisches Institut der Staedlischen Kliniken, *Beurhausstr. 40, 4600 Dortmund, Federal Republic of Germany*

At the Institute of Pathology of the Clinic at Dortmund, the Hauptverband der Gewerblichen Berufsgenossenschaften has opened a central register for all cases of mesothelioma. The Berufsgenossenschaft will request lung material for analysis from the surgeons and pathologists.

481. RELATION OF PLEURAL THICKENING AND PLEURAL PLAQUES TO MESOTHELIOMA IN FORMER ASBESTOS WORKERS

Smither, W. J., Hanson, A., East Ham Memorial Hospital, Chest Clinic, *Katharine Rd., London E16, England, United Kingdom*

OBJECTIVE: Annual review of cohort of former asbestos workers by chest X-ray, clinical examination, lung function.

482. BRONCHUS CARCINOMA IN URANIUM MINERS (SCHNEEBERGER LUNGENKREBS)

Hain, E. F., Ulmer, W. T., Kalthoff, J., Allgemeines Krankenhaus, Dept. of Pneumology, *Bissendorfer Pferdeweg 52, 2000 Hamburg 90, Federal Republic of Germany*

Bronchus carcinoma is being studied in 47 cases found in uranium miners in the Federal Republic of Germany after the Second World War. 45 of these persons were exposed to uranium in Saxony/Bohemia outside the Federal Republic of Germany. All data, especially the radiation measurements, of these miners are kept secret, so that it is impossible to measure the real radiation exposure. This is estimated by the time of exposure to uranium. No control group is used because of this lack of information. Besides time of exposure the following data are collected: age at death, latency period, place and type of uranium mining, therapy, time of survival after discovery of the carcinoma, site and histology of the carcinoma, metastases, clinical data, pneumoconiosis, and smoking history.

483. CYTOLOGICAL SCREENING FOR LUNG CANCER IN WORKERS EXPOSED TO HEXAVALENT CHROMIUM IN A CHEMICAL PLANT

Herivan, R. M., Horvath, P., Ministry of Chemical Industry, Labour Protection & Hygiene Centre, Lab of Cytology, *59 Pop de Basesti, 73244 Bucharest 3, Romania*

The object of the study is to monitor 50 workers exposed to hexavalent chromium in a department in which chromium catalyst is manufactured, using cytological screening of sputum for the early detection of lung cancer as well as of epithelial disorders which may precede the development of a tumor. Annual cytological screening of sputum collected for three consecutive mornings and kept in Eskenasy fixative solution is carried out. Paraffin was added and the sputum dyed with HE and Masson. Results are correlated with age, sex, smoking habits, length of exposure, pulmonary antecedents, and exposure levels.

484. URINARY CYTOLOGICAL INVESTIGATIONS FOR DETECTION OF BLADDER CANCER AMONG RUBBER WORKERS EXPOSED TO PHENYL-2-NAPHTHYLAMINE

Herivan, R. M., Ministry of Chemical Industry, Labour Protection & Hygiene Centre, Cytology Laboratory, *59 Pop de Basesti, 73244 Bucharest 3, Romania*

The objective is to monitor the incidence of urinary bladder cancer in subjects exposed to phenyl-2-naphthylamine in the rubber industry. Cytological exfoliative screening with Giemsa stain and Papanicolaou's classification is used for early detection.

485. PILOT STUDY FOR THE EARLY DETECTION OF LARGE BOWEL CANCER IN AN OCCUPATIONAL HEALTH SETTING

Silman, A. J., Nicholls, R. J., University of London, London Hospital Medical College, Dept. of Clinical Epidemiology, *Turner St., London E1 2AD, England, United Kingdom*

OBJECTIVES: 1) To compare the use of occult blood testing with a questionnaire designed for personal completion as a method of screening for large bowel cancer. 2) To assess the acceptability of screening for large bowel cancer in a working population.

APPROACH: A questionnaire, designed for patient completion, covering symptoms of large bowel disease has been successfully piloted in a group of new outpatient attenders. Its estimated sensitivity and specificity suggested that it would be useful for general screening.

Two occupational groups have been selected: one from a light engineering factory, the other from a public service institution; both with approximately 1000 employees over 40 years of age. All employees will be invited to complete a questionnaire and provide 6 samples of stools for testing by Hemoccult.

Letters, meetings and similar activities will be introduced to encourage a high acceptance. Any positives on either Hemoccult or questionnaire will be referred directly to a special clinic for further investigation. This will include a flexible sigmoidoscopic examination in every case, and, where appropriate, a Barium enema.

All negatives on screening will be rescreened after a six-month interval.

486. QUANTITATIVE MICROSCOPY

Young, University of California, Central Office, Lawrence Livermore Lab., *P.O. Box 808, Livermore, California,* 94550, United States of America

This project will establish a coordinated program for the early detection of serious and delayed health effects, including cancer and mutation, in workers and other persons at risk for significant exposure to noxious pollutants from fossil fuel technologies. A battery of tests will be applied to samples of blood, urine, and semen. The tests will measure chromosome aberration and sister chromatid exchange rates, frequency of mutant hemoglobin in red cells, enzyme and apolipoprotein profiles of

serum, mutagenicity, enzyme profile and cytological abnormality in urine, and frequency of abnormal sperm. These tests currently are in use under development in this laboratory, and they all are designed to detect precancerous lesions and genetic damage in man. Their application will allow detection of hazardous situations early enough to take remedial action and to safeguard the health of the individual and society. This project will: (1) identify those tests that measure significant genetic and carcinogenic effects induced by exposure to fossil fuel pollutants; (2) validate the epidemiology and dose-response of the tests; and (3) apply the tests as personal dosemeters to monitor exposure of workers for potential health effects caused by fossil fuel pollutants.

487. HEALTH EFFECTS OF FOSSIL FUEL PROCESSES

Mayall, B. H., University of California, Central Office, Lawrence Livermore Lab., *P.O. Box 808, Livermore, California*, 94550, United States of America

This project establishes a coordinated program for the early detection of delayed and potentially serious effects on human health of exposure to noxious agents. A battery of tests designed to detect precancerous lesions and genetic damage are applied to samples of blood, urine, and semen. The samples are obtained from workers and other persons at risk based on their significant exposure to noxious pollutants from fossil fuel technologies. The tests currently are in use or are under development, and measure: sister chromatid exchange rate; incidence of erythrocytes with mutant hemoglobin; proteolytic enzyme profiles of serum; mutagenic activity of serum and urine; urinary cytology; and frequency of abnormal sperm in semen. Test results are correlated with epidemiological input concerning donor health and medical, workplace, and exposure history, etc. We propose a longitudinal study of oil refinery workers, grouped into cohorts at high or low risk for exposure to noxious agents. Individuals will be tested annually for sister chromatid exchanges, urinary cytology, sperm morphology, etc. Results will be compared between cohorts and will be correlated prospectively for individual exposure and subsequent health status.

488. LUNG CANCER SCREENING OF WORKERS AT HIGH RISK

Mittman, C., Taylor, J. C., Todd, C., Teplitz, R., Gildenhorn, H., Madison, R., City of Hope Medical Center, Dept. of Respiratory Disease, *1500 E. Duarte Rd., Duarte, California*, 91010, United States of America

Through a longitudinal study of approximately 6000 coke-oven workers we will characterize the histopathology of lung cancer occurring in this high-risk occupation and determine if repeated sputum cytology studies reveal a sequence of changes leading to lung cancer. We seek also to determine if coke workers who develop lung and other cancer have elevated levels of tumor markers such as serum CEA, serum and urine polyamines. We will try to ascertain if the presence of tetraploidy characterizes cells in lung cancer. Factors influencing these changes will be examined, especially cigarette smoking history, job location and duration. This information will be used to propose cancer control strategies for this group of workers.

489. SPUTUM CYTOLOGY RELATED TO A FOUNDRY EXPOSURE

Simard, A., Band, P., Vauclair, R., Poquette, G., Saccomanno, G., Cole, P., Institut du Cancer de Montreal, Centre Hospitalier Notre Dame, *1560 Sherbrooke St. E., Montreal, Quebec*, H2L 4M1, Canada

Some studies have shown an increased risk of lung cancer among foundry workers. Sputum cytology among uranium miners has shown cellular changes ranging from mild, moderate and marked atypia to cancer in-situ and invasive cancer. Sputum cytology will be undertaken in 700 foundry workers, using the technique of Saccomanno. Results will be related to duration of exposure in the foundry. Information on age, date of entry into the industry, work history, and smoking history will be obtained and person-years at risk evaluated. Comparisons will be made with other exposed groups, namely uranium miners, asbestos workers and smokers.

490. PULMONARY MINERAL FIBERS AND LUNG CANCER

Churg, A. M., University of British Columbia, Dept. of Pathology, *6174 University Blvd., #300, Vancouver, British Columbia*, V6T 1W5, Canada

This project attempts to determine if the particulate component of air pollution, specficially the fibrous mineral component, can be correlated with the presence of lung cancer. The project utilizes a case/control method. Mineral fibers are extracted from lungs of lung cancer patients and matched (age, sex, smoking, occupational group) controls. Fibers are counted, measured, and identified using electron optical techniques. Statistical correlations are attempted for a variety of fiber parameters (number, mineral type, size, aspect ratio) and combinations of parameters and the test and control groups compared.

491. INVESTIGATION INTO THE USE OF MALIGNANT CELL CYTOLOGY SCREENING FOR BLADDER CANCER IN A CHEMICAL COMPANY

Cartwright, R. A., Gadian, T., Garland, J. B., Yorkshire Regional Cancer Org., *Leeds LS16 6QB, England, United Kingdom*

Routine screening has been undertaken by a chemical company since 1952. The firm had produced carcinogens but stopped production before that date. The aim of the study is to assess the survival of workmen diagnosed as having bladder cancer after screening as contrasted to those presenting symptomatically. All cases of bladder cancer in workmen have been identified and details of screening recorded as well as their outcome. Cases not industrial in origin but treated contemporaneously have been identified elsewhere in the city and used as a matching group in terms of treatment regimens. The study awaits a few details of follow-up before completion.

492. HEMOCCULT TEST IN THE SCREENING OF COLORECTAL CANCER IN OCCUPATIONAL GROUPS

Lambert, R., Stremsdoerfer, N., Centre National de la Recherche Scientifique, Centre d'Epidemiologie, *8 ave. Rockefeller, LP No. 005440 c/o Fac. Med., 69008 Lyon, France*

The aim is to evaluate the efficiency of the Hemoccult test in the detection of tumoral colorectal lesions (adenoma and cancer). The survey will be conducted in occupational groups concerned with chemicals (drug companies, petrochemicals and polymers, mineral compounds situated around Lyon). The test group consists of 1,600 persons. A questionnaire on intestinal symptoms is administered and Hemoccult testing is carried out. Positive subjects will be explored. The incidence of colorectal lesions in a control group of 2,000 will be followed.

493. RADIOIMMUNOASSAY OF CEA AND AFP AS A SCREENING TEST IN THE SURVEY OF HEALTH OF WORKERS IN THE CHEMICAL INDUSTRY

Ivanescu, M. A., Mihaela, B., Marie, P., Alexandru, T., Ministry of Chemical Industry, Labour Protection & Hygiene Centre, Radioimmunoassay Laboratory, *59 Pop de Basesti, 73244 Bucharest 3, Romania*

Selected groups of workers with exposure to vinyl chloride, benzene, chromium, amino compounds, and black carbon have been examined since 1975 by radioimmunoassay techniques. The results are correlated with numerous laboratory and clinical data in order to evaluate the possibility of using RIA of serum or urine CEA and AFP as a screening test in the survey of health of groups of workers with occupational cancer risk.

494. SCREENING FOR BOWEL CANCER - STUDY OF A POSSIBLE CORRELATION WITH EXPOSURE TO CUTTING OILS

Thony, C. C., Bonnavion, J., Centre de Medecine du Travail, *20 rue du Pre Benevix, Cluses, France*

3,000 males aged 40 years and over are screened by means of the hemoccult test. Positive cases are examined by endoscopy and X-ray. The incidence of exposure to oil vapors (inadvertently swallowed) is being determined.

495. PROSPECTIVE STUDY OF OCCUPATIONAL LUNG CANCER

Baganha, M. F., Bernarda, R. A., Figueiredo, F., Rebelo, R. M., Telo Morais, J. C., Reis, M. V., Leal Gonclanes, L. F., Chieira, C. M., Carmo, J. C., Almeida, J. R., Antunes, C. A., Universidade

de Coimbra, University Hospital of Coimbra, Clinica de Pneumologia, *Coimbra, Portugal*

This is a prospective study of workers in a mine with elevated levels of radioactivity involving clinical, radiological, spirometrical, cytological (sputum) and immunological examinations every four months. The results in terms of lung cancer will be compared with those of a group of control workers, who will undergo the same examinations. Both cases and controls will be asked in detail about smoking habits.

496. DETERMINATION OF TOBACCO SMOKE METABOLITES IN URINE AND BLOOD

Baksaas, I., Langard, S., Torgrimsen, T., Telemark Sentralsjukehus, Dept. of Occupational Medicine, *Olavsgt. 26, 3900 Porsgrunn, Norway*

OBJECTIVES: Phase I: To determine metabolites of tobacco smoke in urine and blood. Phase II: Use of metabolite studies to identify indicators characteristic of individuals with high risk of cancer.

APPROACH: I) Metabolites are going to be determined in urine and blood of heavy smokers and non-smokers. The metabolites will be studied by gas chromatography with flame ionization/electron capture detector, high-pressure liquid chromatography with variable UV/fluorescence detector and by mass spectrometry. II) The same procedures are to be applied for screening of metabolites in already identified tobacco smoke-exposed population and industrial-exposed population.

VII. BROAD PROGRAMS ON OCCUPATIONAL AND ENVIRONMENTAL CARCINOGENESIS

497. PILOT STUDIES DEMONSTRATING THE FEASIBILITY OF OZONATION FOR SELECTED MUNICIPAL WATER SUPPLIES

Rollag, D. A., South Dakota State University, School of Engineering, Dept. of Civil Engineering, *Brookings, South Dakota*, 57006, United States of America

The detection in drinking water of possible carcinogens such as chloroform, an end-product of chlorine disinfection, has stimulated an interest in ozone as an alternative. The increased cost and real or threatened shortages of chlorine and development of more dependable, less costly ozonators have also contributed to this trend. As a result, there is a considerable amount of research in progress directed toward the basic chemistry, toxicology, and end-product formation of ozone. However, there is an apparent gap between these rather fundamental areas and the application of ozone in everyday treatment of water. This research is intended to help bridge this gap.

These studies will be conducted on both surface and groundwater supplies of five South Dakota communities. A portable, pilot-scale ozonation plant would treat each water supply at various ozone dosages and contact times. For each steady-state run, flow, power input, temperature, pH, turbidity, ozone input and residual would be measured along with total coliform, standard plate counts, iron, manganese, taste, color and chloroform. These data will be evaluated to: (1) determine the ozone demand, optimum dosage and contact time for disinfection and removal of iron, manganese, taste, odor and color; (2) establish the capital and annual costs of ozonation for comparison with other treatment alternatives; (3) evaluate the potential of ozonation for reducing formation of chloroform; and (4) demonstrate the use and costs of ozonation to water utility personnel.

498. EFFECTIVENESS OF ACTIVATED CARBON FOR REMOVAL OF TOXIC AND/OR CARCINOGENIC COMPOUNDS FROM WATER SUPPLIES

Weber, W. J., University of Michigan, Ann Arbor Campus, School of Engineering, Dept. of Civil Engineering, *Ann Arbor, Michigan*, 48104, United States of America

The complex problem of trace organic contaminants in water supplies can be broadly divided into two major categories: 1) naturally occurring organic substances that are transformed to potentially more harmful species by water treatment operations such as chlorination; and 2) compounds of industrial, agricultural and other man-related origin that are now indigenous to many raw water supplies and which resist removal by conventional water treatment practices.

Substantial effort is being directed by the U.S.E.P.A. to resolution of problems associated with the first category of compounds; one potential solution is to use activated carbon treatment in advance of chlorination to eliminate the precursor compounds. The proposed research will be directed to removal of the second category of contaminants, to an evaluation of the competitive effects that naturally occurring organics have on the effectiveness of carbon for removal of the second category of contaminants on a long-term continuous basis, to the effects that other major water treatment operations have on this effectiveness, and to quantification of the associated adsorption dynamics to facilitate optimum design and application methodology.

PROGRESS: Batch adsorption tests have been completed for all test materials; humic acid, dieldrin, carbon tetrachloride, PCB, p-dichlorobenzene, benzene, column studies are completed or ongoing. Predictive modeling attempts are underway; biological activity is having considerable influence on the results and is causing difficulties with the adsorptive process modeling efforts.

Final report is being prepared.

499. REMOVING ORGANIC CONTAMINANTS FROM DRINKING WATER - A PILOT PLANT STUDY

Wood, P. R., Morgan, R. A., Waddell, D. H., State University System of Florida, Florida International University, Graduate School, *Miami, Florida*, 33199, United States of America

OBJECTIVES: A 100 gal. per minute pilot plant study to devise feasible and economic methodology for full scale plant removal of existing organic contaminants from ground water and/or prevent development of potential carcinogens in the public water supplies in Dade County, Fla. The findings will also be applicable to other areas.

APPROACH: Various types of granular activated carbon will be studied for effectiveness in removing precursor substances which react with chlorine to produce potential carcinogens, and in removing existing contaminants present in the ground water and contaminants formed in the plant process. Optimum placement of carbon adsorbers, carbon life and regeneration, effect of ozone, ultraviolet light and bacteria will be studied. In addition, lower cost methods of minimizing contaminants by coagulation and disinfection modifications will be studied.

PROGRESS: Investigation of four activated carbons using parallel pilot columns has been completed. These carbons were compared for adsorption of TOC, THmFP, halogenated and non-halogenated purgeables. Based on results from these comparisons a carbon was selected for the next phase of pilot column studies.

500. ENVIRONMENTAL HEALTH SCIENCES CENTER

Wogan, G. N., Louis, J. F., Beer, J. M., Brunengraber, H., Biemann, K., Steinfeld, J. I., Busby, W., Gelbard, F., Howard, J. B., Longwell, J. P., Merrill, E. W., Sarofim, A. F., Massachusetts Inst. of Technology, Harvard M.I.T. Program in Health Sciences & Technology, Dept. of Nutrition & Food Science, *77 Massachusetts Ave., Cambridge, Massachusetts*, 02139, United States of America

The overall objective is to develop a series of data bases on which assessment of potential health consequences, especially total burden of environmental carcinogens and mutagens, resulting from utilization of fossil fuels can be made more objectively and with greater precision than is currently possible. The program of research has the objective of determining the character and range of potential health effects associated with several technologies for fossil fuel combustion by relating evaluations of a variety of biological responses to critical operating parameters characteristic of existing and alternative combustion equipment.

The ultimate aim is to define conditions of combustion for each of several fuel types which result in the emission of minimal amounts of substances with mutagenic and/or carcinogenic properties. This objective is being approached through the following lines of investigation: (1) Conducting parametric combustion studies using laboratory and larger-scale combustors to

determine effects of temperature, equivalence ratio and fuel type on the formation of particulates and polycyclic compounds. (2) Subjecting selected samples from the combustion experiments to exhaustive chemical analysis. (3) Evaluating the biological and biochemical properties of selected samples produced under defined combustion conditions with respect to mutagenicity in bacteria and human cells and ability to form covalent adducts with nucleic acids when activated in vitro and in vivo.

501. MOLECULAR PERTURBATIONS IN MAN PRODUCED BY ENERGY RELATED POLLUTANTS

Anderson, N. G., U.S. Dept. of Energy, Div. of Biological & Medical Research, *9700 S. Cass Ave., Argonne, Illinois*, 60439, United States of America

Radiation and energy-related toxic agents may produce a variety of biological effects including DNA breakage, altered DNA repair, mutation, altered gene expression, cancer, or cellular toxicity, accelerated aging, and cell death. These effects can only be understood in terms of a wide range of molecular mechanisms involving the estimated 30 to 50,000 protein gene products (PGP's) encoded by the human genome. We have developed the systems and techniques required to see a large fraction of all human PGP's and to index them in a rational manner. This makes possible a revolution in energy-related biomedical research since effects may now be studied in terms of specific molecular species. For the study of PGP's we have developed mapping systems and techniques for using high resolution two-dimensional electrophoresis techniques for spot identification, for determining a number of identifying biophysical properties and compositional characteristics for each PGP, and for image analysis and data reduction. Maps and multiple identifications for PGP's in human plasma, muscle red cell lysates, and urinary protein concentrates have been prepared and published. Emphasis now centers on the indexing of PGP's of human peripheral lymphocytes, and on changes in the pattern of gene expression in these cells in response to radiation, carcinogens, toxic chemicals, and hormones.

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502. ENVIRONMENTAL HEALTH SCIENCES CENTER GRANT

Selikoff, I. J., Langer, A. M., Lilis, R., Nicholson, W. J., Hammond, E. C., Suzuki, Y., City University of New York, Mount Sinai School of Medicine, School of Medicine, Dept. of Community Medicine, *1 Gustave L. Levy Pl., New York, New York*, 10029, United States of America

Both epidemiological and laboratory research are integrated to investigate human health effects of environmental agents. Studies continue to be concentrated in several areas: low-level, long-term exposure to xenobiotics; multiple factor interaction of environmental agents; environmental cancer; asbestos-associated disease; biological effects of inorganic microparticles; halogenated aromatic hydrocarbons (including polychlorinated biphenyls, polybrominated biphenyls, pentachlorophenols, dioxins, dibenzofurans, etc.). In addition, other occupational hazards (particularly work accidents) are being investigated to seek additional information concerning possibilities of prevention. During 1980-1981, a significant extension of the research programs will take place, in the preparation of a prospective pair of surveillance programs of two groups at very high risk of development of cancer; asbestos insulation workers and roofing workers exposed to complex polycyclic aromatic hydrocarbons. Clinical examinations to be undertaken at a variety of sites in the United States will establish baseline observations, including those associated with what may be predictive biological markers, for subsequent prospective observation.

Agents being investigated include titanium, lead, fluorine, polychlorinated biphenyls, polybrominated biphenyls, nitrosamines, dioxins, asbestos, nickel, cadmium, vinyl chloride, zeolites, and solvents.

BIBLIOGRAPHIC REFERENCES: Fischbein, A., Thornton, J., Wolff, M.S. and Selikoff, I.J. Dermatological findings in capacitor manufacturing workers exposed to dielectric fluids containing polychlorinated biphenyls (PCBs). Acta. Derm. Venereol. 1980., in press. Fischbein, A., Thornton, J.C., Lilis, R., Valciukas, J.A., Bernstein, J. and Selikoff, I.J. Zinc protoporphyrin, blood lead and clinical symptoms in two occupational groups with low-level exposure to lead. Amer. J. Indus. Med. 1980., in press.

503. ECOLOGICAL, STATISTICAL, ETHOLOGICAL, AND RELATED BIOLOGICAL STUDIES ON AIR POLLUTION, SMOKING AND OTHER ENVIRONMENTAL VARIABLES (ABBREV)

Hickey, R. J., Clelland, R. C., Spence, D. E., Bowers, E. J., Clelland, A. B., University of Pennsylvania, Wharton School of Finance & Commerce, Dept. of Statistics, *34th & Spruce Sts., Philadelphia, Pennsylvania*, 19104, United States of America

Statistical and other studies are being conducted to test a four-part hypothesis that: (1) Among common air pollutant chemicals there are some that are mutagenically or otherwise hazardous to health; (2) such chemicals accelerate development of and increase risk of occurrence and mortality from chronic diseases of aging (e.g., cancer, heart disease), and also alter intergenerational DNA leading to birth defects and their consequences, in proportion to exposure; (3) chronic disease risk and resultant mortality are influenced significantly by individual genetic/constitutional characteristics; and (4) these individual characteristics also significantly influence certain behavioral physiological characteristics, such as tobacco smoking and coffee drinking. Three subsidiary hypotheses are that (5) smoking is, for many, symptomatic of physiological deficiencies that nicotine tends to alleviate, with smoking functioning partly as an example of behavioral regulation of physiological homeostasis, (6) viruses can also function mutagenically, along with certain environmental pollutant chemicals, leading to accumulation of somatic mutations, and (7) recent urban mortality rate data are more strongly correlated with air pollution levels of, say, 10 years ago than with recent levels. The basis for (7) may be a result of cumulative, and possibly multiplicative (cf. Orgel's theory), long-term effects of cell alterations inflicted by pollutant chemicals and other factors, including viruses. Methods of multivariate statistical analysis are used in these multi-regional, multi-environmental variable studies, especially an optimal subset selection (algorithm) modification of multiple regression analysis. Data used are human mortality rates for all cancers, cancers of various sites, and leukaemia, along with other chronic diseases (e.g., heart disease) for individual metropolitan populations, and environmental chemical concentration data and other environmental variable data.

504. OCCUPATIONAL AND ENVIRONMENTAL HEALTH

Whittenberger, J. L., Brain, J. D., Eisenstadt, E., Ferris, B. G., Godleski, J., Baker, E. A., Harvard University, Boston Campus, School of Public Health, Dept. of Physiology, *55 Shattuck St., Boston, Massachusetts*, 02115, United States of America

This research and research training program emphasizes a variety of laboratory studies and epidemiologic approaches to the study of the effects of environmental and occupational factors on the health of man. Specific examples include the following: biology of alveolar macrophages as a pulmonary defense mechanism; effects of breathing pattern and lung volume on the distribution of inhaled particles; development and exploitation of differentiated mammalian cell culture systems to detect, examine the mechanisms of action, and develop means for prevention or reversal of certain environmental chemical toxic agents; development of new chemical and immunologic assay methods for certain classes of environmental chemicals; development and use of affinity probes to identify the sites and molecular mechanisms of action of specific toxic agents; malignant transformation in vitro; cancer morbidity and mortality among rubber workers; pulmonary function changes in granite dust exposures, toluene di-isocyanate exposures, and other occupational exposures; the uses of proportional mortality analysis in identifying suspected occupational exposures; a prospective study of children and adults exposed to specific indoor and outdoor air pollutants.

505. CONDUCT OF RESEARCH ON OCCUPATIONAL CARCINOGENESIS

Bridbord, K., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, *5600 Fishers Ln., Room 3-32, Rockville, Maryland*, 20852, United States of America

OBJECTIVE: This agreement was originated as a congressionally mandated effort to integrate and thereby enhance the activities of both the National Cancer Institute and the National Institute for Occupational Safety and Health in investigating chemical related occupational cancer.

MAJOR FINDINGS: To date some 71 distinct projects have been initiated, of which approximately 50 are in progress. Most of the projects were reported on in a combined NCI/EPA/NIOSH Collaborative Workshop held in April, 1980.

SIGNIFICANCE TO BIOMEDICAL RESEARCH AND PROGRAM OF THE INSTITUTE: The merging of the unique capabilities of each organization into a concerted investigation of a variety of industrial situations promises an acceleration of the response to the question of the quantification of occupationally caused cancer. In that quest, answers to the many questions concerning acute toxicity, safe ambient levels, etc., which are more germane to the NIOSH mission, will accrue. NIOSH contributes the capability of freely entering industrial operations as well as considerable experience in surveying potentially dangerous situations therein.

PROPOSED COURSE: The ongoing projects shall be continued as dictated by their objectives and workscopes. New projects shall be begun as a result of initiation by the staff of either organization and relevance and technical review by a combined ad hoc committee of the senior staff members of both institutes. Obligation of funds by the NCI for the ensuing fiscal year shall in no case exceed the sum of four million dollars.

506. ID OF OCCUPATIONS AT HIGH RISK FROM SYNERGISTIC EFFECTS - NCI

Hills, Venable, U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Div. of Surveillance, Hazard Evaluations & Field Studies, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

Combined industrial exposures are extremely common in the workplace, but are rarely specifically studied, because it is far easier to separate out a single toxic component and to define and study its effects that it is to identify the net effects of combined exposures.

There are numerous examples of two or more chemicals or physical agents interacting synergistically to produce a range of deleterious health effects. It is commonly recognized that certain classes of substances act as cocarcinogens, tumor promotors, initiators, or potentiators. Examples of cocarcinogens include asbestos and tobacco smoking, carbon tetrachloride and UV radiation, benzopyrenes and sulfur dioxides, benzopyrenes and diol epoxides. There are also examples of two chemical agents forming, under workplace conditions, a third compound which is carcinogenic, e.g., hydrogen chloride and formaldehyde combining to form bis(chloromethyl)ether (BCME). The formation of nitrosoamines in cutting oils, tumbling compounds, and drawing agents from nitrites and secondary and tertiary amines is yet another example.

Certain host factors such as dietary patterns and drug regimens can predispose an exposed worker to a greater risk than would be expected from simple exposures to the occupational hazard. Examples include caffeine and noise, antabuse and either carbon disulfide or ethylene dibromide, alpha-1-antitrypsin deficiency and welding fumes.

There are also instances where the environment serves to increase an agent's potential for health effects. Examples include sunlight and creosote, sulfur dioxide plus sodium chloride aerosol plus high humidity, and solvents with high temperatures.

This project will identify occupational groups where the potential for synergistic effects is high.

507. WORK HAZARD INFORMATION AND EDUCATION PROGRAM ON OCCUPATIONAL CANCER

Wright, C., U.S. Dept. of Labor, Occupational Safety & Health Admin., *200 Constitution Ave. N.W., Washington, District of Columbia,* 20210, United States of America

OBJECTIVES: (1) To support those New Directions Grants or parts of grants awarded by OSHA which relate to occupational cancer. (2) To support an Asbestos Alert Program for current workers exposed to asbestos and their families. (3) To support the development of audiovisual materials on safe procedures for the removal or containment of asbestos in schools and other buildings. These are to be used for the education of state and local departments of health and education, local school boards, architects, contractors and their employees regarding the measures required for protection against asbestos exposures during such procedures.

ACCOMPLISHMENTS: This is the second IA with OSHA which has been initiated by the DCCR, NCI. The first, initiated in 1976, was an effort to increase the awareness of workers regarding occupational cancer hazards through the establishment of a cancer information and alert program and the development of education materials for several categories of workers at high risk for cancer because of occupational exposure to carcinogens. Workers receiving special attention were those in the metal smelting, coke oven, rubber, asbestos and petroleum industries.

The second IA was negotiated in 1978 to provide some NCI support for part of the New Directions Grants Program which had been authorized by Congress. Since OSHA has developed effective channels for cooperation with labor groups, it seems more appropriate for NCI to pursue its goals in prevention, detection and treatment of occupational cancer through OSHA than to try to develop separate contracts and programs. These grants were made to unions, other labor groups, academic institutions and foundations which wanted to provide educational programs about occupational safety and health hazards to workers. DCCR, NCI, agreed to support those grants or parts of grants which were concerned with cancer risks.

In FY '80, the second IA was enlarged to include: (1) An increase in support to the cancer-related parts of the New Directions Grants; (2) the Asbestos Alert II plan, a public media campaign to be launched January 1981, which will be targeted to current workers and their families; and (3) a special program to develop audiovisual materials for state and local departments of health and education, architects, contractors and their employees. (Text Abridged.)

508. CANCER RISK CONTROL BY BEHAVIORAL METHODS

Smith, M., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Biomedical & Behavioral Science, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

This project seeks to synthesize and apply behavioral science principles for motivating workers to utilize appropriate hazard control procedures when working with carcinogens. Treating styrene as a model substance, a four year contract (210-77-0040) was awarded at the end of FY 77 to develop appropriate work practices for handling and working with this chemical in the boat building industry, and for motivating worker usage of these work practices in selected plants. Both worker training and a financial incentive system for compliance with proper work proctices will be used to motivate workers' usage. A pilot study has been performed which found that introduction of certain work practices to take better advantage of ventilation reduces workers' exposure to styrene by 50 percent.

An elaborate set of suggested work practices for mininmizing risk of styrene exposures has been now developed and contacts made with establishments using this material to undertake a full-scale evaluation of their effectiveness. Necessary training and motivation programs are being implemented in one test plant with the first evaluations to be made during FY 80.

In addition to its use as a fibrous glass hardening agent, styrene is present in many rubber and plastic manufacturing processes. Overall, the population at risk is estimated at 500,000 workers.

509. ENVIRONMENTAL CANCER PREVENTION AND LABOR HEALTH EDUCATION

Wang, V. L., Zapka, J., Li Scholz, A., Gotti, R., French, R. M., Johns Hopkins University, School of Hygiene & Public Health, Dept. of Health Services Administration, *615 N. Wolfe St., Baltimore, Maryland,* 21205, United States of America

This proposal addresses the development of an educational program for workers on occupational and environmental carcinogenic hazards.

The program has two major objectives: 1. The development of a relevant health education model for the college-bound industrial workers with the expectation that they will in turn impact on co-workers, management and the community. 2. The identification of mechanisms and linkages by which cancer prevention information can be disseminated to workers.

Drawing on the expertise of the Johns Hopkins School of Hygiene and Public Health, the Johns Hopkins Occupational Safety and Health Education Resource Center, the Johns Hopkins Oncology Center and the educational resources of Empire State College, the project team will focus on the Empire State College Center of Labor Studies to develop the model program. This Center has a present study body of approximately 1,500 representing over 50 labor unions. Through working with such a student body, the project team will be able to develop and evaluate methods and materials relevant to the specific needs and problems of workers for occupational and environmental related cancer prevention.

510. RESPIRATOR AND CLOTHING RESEARCH FOR CARCINOGENS - NCI

Todd, W., U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health, Division of Biomedical & Behavioral Science, *4676 Columbia Pkwy., Cincinnati, Ohio,* 45226, United States of America

Ongoing cancer research has shown more and more of the chemicals encountered in the work environment to be suspected carcinogens. Since personal protective equipment plays a major role in worker safety, evaluations of the protection afforded by such equipment must be made. It has been found that the typical respirator sorbent, charcoal, is not effective against certain suspected carcinogens. Also, little work has been done regarding the performance of protective clothing against carcinogenic materials. NIOSH has an obligation to insure adequate performance of personal protective equipment recommended for health standards.

An IAA was negotiated with DOE/LASL to perform a study of carcinogen permeation through protective clothing and to evaluate commercial respirator cannisters against Class I and suspect carcinogens and to develop an improved sorbent for vinyl chloride. A special study of benzene permeation through protective clothing was negotiated at an additional cost.

The DOE/LASL IAA (79-13) will be completed and no additional work is planned in this area in FY 81 by DPSE.

511. PERSONNEL AND PLANT MONITORS

D'Silva, A. P., Fassel, V. A., Iowa State University of Science & Technology, U.S. Dept. of Energy Ames Lab., *University Station, Box 14A, Ames, Iowa,* 50010, United States of America

Fossil fuel conversion and shale oil extraction technologies pose substantial environmental and occupational hazards through potential fugitive emissions of toxic and carcinogenic substances. For in-plant environments, the substances of primary concern are hydrocarbons (benzene), polynuclear aromatic hydrocarbons (benz(a)pyrene), heterocyclic compounds, organometallic trace elements (e.g., Ni(CO)4), and inorganic species containing trace elements (e.g., AsH3). Personnel working in the environments of coal conversion plants may thus be simultaneously exposed to a wide array of substances that contain known or potential carcinogens, co-carcinogens, mutagens and oncogens. Because cocarcinogens that by themselves are non or weakly carcinogenic can enhance the potency of known carcinogens, multipollutant plant and personnel monitoring systems are needed to assess the toxic or carcinogenic index of a plant environment. Thus, we propose to develop: (1) single species monitors, e.g., C6H6, benz(a)pyrene, AsH3 etc.; and (2) biochemical Carcinogenic Index monitors that are primarily based on luminescence phenomenon.

512. EVALUATION OF OCCUPATIONAL HAZARD MONITORING SYSTEMS

Bell, J., Inst. of Cancer Research, Division of Epidemiology, *Clifton Ave., Sutton SM2 5PX, England, United Kingdom*

The establishment of information systems for monitoring health of employees (particularly in the oil and chemical industries and those using their products) is under consideration and, in some cases, implementation. However, it is not clear a priori what data must be collected and how they should be analyzed to highlight hazards. Computer simulation of an industrial hazard monitoring system is proposed to answer these questions and to evaluate the potential usefulness of the various systems that have been suggested.

513. WORKER NOTIFICATION AND INFORMATION PROGRAMS

Polakoff, P. L., Western Inst. for Occupational & Environmental Sciences, Environmental Service, *2001 Dwight Way, Berkeley, California,* 94704, United States of America

OBJECTIVE: Develop effective strategies for notifying and informing workers, ex-workers, and other relevant individuals, concerning their exposure to an occupationally related carcinogenic substance. Effective strategies would be viewed as those most likely to ensure that the information actually reaches the target population and persuades them to adopt risk-reducing behavior.

514. RESEARCH IN ENVIRONMENTAL HEALTH SCIENCES

Upton, A., Albert, R. E., Pulmes, E. D., Eisenbud, M., Altshuler, B., Troll, W., Van Duuren, B. L., New York University, School of Medicine, Dept. of Environmental Medicine, *100 Washington Sq. E., New York, New York,* 10003, United States of America

This grant provides core support for a broad program in the Environmental Health Sciences. The research under way and proposed is broadly relevant to adverse health effects from Environmental factors. The general objectives of the research are to define the nature and extent of such effects with the aim of instituting appropriate preventive or control procedures where required. Interests range from acute to chronic health effects including, in the latter, cancer and the degenerative diseases.

The research encompasses laboratory studies on the biochemical mode of action of environmental toxicants, exploratory studies aimed at improving the reliability and efficiency of predictive toxicological tests, improvement of diagnostic procedures for disease possibly related to environmental factors, epidemiological investigations and field studies on the distribution of pollutants.

515. RESEARCH IN ENVIRONMENTAL CANCER

Nelson, N., Albert, R. E., New York University, School of Medicine, Dept. of Environmental Medicine, *100 Washington Sq. E., New York, New York,* 10003, United States of America

This proposal seeks continued support for an NCI Center Grant entitled 'Research in Environmental Cancer.' This Center Grant provides core support for the Institute in the area of cancer research including partial salary support for professional staff, developmental funds, and limited support for items of shared equipment and central services. The research and teaching program in cancer at the Institute has the broad objective of identifying environmental causes of cancer and developing methods for the control of carcinogenic hazards. The program is interdisciplinary in character and ranges from studies at the subcellular level on mechanisms of action to whole animal, epidemiological and environmental studies.

516. RISK ASSESSMENT FOR ENVIRONMENTAL CARCINOGENS

Hoel, D. G., Hogan, M. D., Kaplan, N. L., Perez, C. A., Poon, A. H., Portier, C., Anderson, M. W., U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Environmental Health Sciences, Biometry Branch, *P.O. Box 12233, Research Triangle Park, North Carolina,* 27709, United States of America

The main objective of this project is to develop improved statistical techniques for using data from animal carcinogenicity tests conducted at high dose levels to estimate long-term human risk from chemical carcinogens at very low dose levels. Current research efforts are focusing on a variety of issues such as competing risk analysis, species-to-species extrapolation, the incorporation of pharmacokinetics in low dose risk estimation, and cancer bioassay design. In addition mathematical models for the genetic effects of radiation have also been considered.

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30, 1979. Hoel, D.G.: Sequential methods in genetic risk assessment. Genetics 92: 196-198, 1979.

517. CANCER CENTER SUPPORT (CORE) GRANT

Wynder, E. L., American Health Foundation Inc., *320 E. 43rd St., New York, New York*, 10017, United States of America

This grant provides funding for principal personnel and central services for the overall prevention-oriented research program at the American Health Foundation. Support services include a research animal facility, and instrumentation, histology, and computer facilities. The Foundation's research program includes projects in cancer epidemiology, chemical carcinogenesis in animal models and cell culture, effects of cigarette smoke and chemical characterization of smoke from various tobaccos, cancer control through risk factor identification and reduction programs in schools and the workplace, and related economic studies. Other laboratory studies cover diet-related investigations of carcinogenesis of the colon, prostate, and other sites.

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CO-INVESTIGATORS:

5) NAME OF FUNDING ORGANIZATION(S) (list principal source first)

6) GIVE MONTH AND YEAR FOR END OF CURRENT FUNDING

7) DESCRIBE PROJECT UNDER THREE HEADINGS: 1) OBJECTIVE; 2) APPROACH; AND 3) PROGRESS [optional] (use specific, technical terms)

PLEASE CHECK ONE: _____ **1. This is a description of a NEW Project.**

_____ **2. This is a REVISED description of Project No.** _____
(Insert identification number)

FORM APPROVED: OMB NO. 068-R1441 EXP. AUG. 1983

CANCER RESEARCH REGISTRY

A Service of the National Cancer Institute

INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM

You are invited to complete a Current Cancer Research Project Registration Form PROVIDED you have NOT completed a similar form for the Smithsonian Science Information Exchange (SSIE), the Clearinghouse for Ongoing Research in Cancer Epidemiology in Lyon, France, or for the Current Cancer Research Project Analysis Center (CCRESPAC) during the last eight months.

Your project description will be entered into the National Cancer Institute's (NCI) data base, CANCERPROJ (Cancer Projects). Your project description will also appear in one or more of the ICRDB publications known as SPECIAL LISTINGs of Current Cancer Research. Every year the ICRDB publishes fifty SPECIAL LISTINGs, each containing project descriptions in different specific oncology research areas. A free copy of a SPECIAL LISTING is automatically sent to each investigator whose project description appears in that SPECIAL LISTING. Thus, investigators are annually made aware of research being carried out in their areas of interest.

GUIDELINES FOR FILLING OUT THE REGISTRY FORM

A. The description should be submitted by or through the individual who is the **principal investigator** of the project described. Major co-investigators should also be listed.

B. If you are working on more than one project, or if your one project consists of several distinct major segments, please prepare a separate summary form for each.

C. Only **CANCER** research projects which are CURRENTLY **ACTIVE** and CURRENTLY **FUNDED** should be submitted.

D. If you are submitting a clinical protocol, please send a copy of the complete protocol. The NCI has an established format which will be used to develop a standard protocol summary. A copy of the prepared summary will be sent to you for review prior to its entry into the data base.

E. Return to address shown on the front of this form.

F. IMPORTANT. If you prefer to have your copy of the SPECIAL LISTING mailed to your home address, or if your co-investigators have different mailing addresses, please list each name and address on a separate sheet of paper.

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